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PNEUMONIA IN PRIVATE PRACTICE

A STUDY OF 911 CASES

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AND
EDGAR A. LAWRENCE, M.D.
NEW YORK

Much has been written in recent times concerning pneumonia especially as regards the incidence of the various types of pneumococcic pneumonia and their amenability to serum therapy. When compared, these reports have shown a rather striking consistency both in the incidence of pneumococcus types and in the results obtained with specific treatment. However, these studies have been based largely on material observed in large city hospitals such as Bellevue and Harlem hospitals in New York and the Boston City Hospital. So far as we know, there have been no modern studies published on pneumonia in private practice. The impression seems to be general, however, that the death rate for pneumonia in private practice is considerably lower than it is in large city hospitals. While in hospital wards the fatality rate may run from 30 to 35 per cent, one often hears practitioners assert that in private practice they rarely lose a patient with pneumonia, and Osler, quoting Howard and Fussell, states that the fatality rate in the latter group varies between 6 and 17 per cent.[1]

In the hope of throwing some additional light on this subject, we have collected 911 cases of pneumonia from private practice. The number of cases included is not as large as we should have liked it to be, but at least it is large enough to form a basis for certain general conclusions.

This study falls naturally into three divisions: (1) patients treated at home, (2) patients treated in the private pavilions of hospitals, and (3) patients seen in consultation in private practice.

PATIENTS TREATED AT HOME

Our original intention was to collect the material for this study from all three of the sources mentioned. We found it almost impossible, however, to obtain adequate records on patients who had been treated in the home. Through the kindness of Dr. Edward S. Rogers, director of the New York State Bureau for Pneumonia Control, we are able to quote the following figures from his investigations in New York State: Rogers found that in 1,475 hospital cases of pneumococcus type I pneumonia the fatality rate was 18.5 per cent, whereas in 551 cases of the same type in which treatment was given in the home the death rate was only 13.4 per cent, a difference of 5 per cent. All the patients in both series received type I serum. These patients were not citizens of New York City but were collected from cities, towns and rural districts in New York State excluding New York City.

The factors that may influence this difference in the fatality rate of patients treated in the hospital and those treated at home will be discussed later.

PATIENTS FROM THE PRIVATE PAVILIONS OF HOSPITALS

The greater part of the material for this study (560 cases) was obtained from the private wards of New York City hospitals. These patients were all admitted during the last decade (1928-1938) and all had been "typed" by standard methods. Many cases of typical lobar pneumonia (more than 50 per cent) had to be excluded from our survey because of inadequate bacteriologic study. The hospitals whose records were used in the compilation were the Doctors' Hospital, Fifth Avenue Hospital, Mount Sinai Hospital, New York Hospital, Post-Graduate Hospital, Presbyterian Hospital and Saint Luke's Hospital, all in the city of New York.[2]

Bacteriologic Classification.—In table 1 it will be noted that approximately 95 per cent of the cases of pneumonia in this series are of pneumococcic origin. This agrees very closely with the observations of Cecil, Baldwin and Larsen[3] in their statistical study of 2,000 cases of pneumonia at Bellevue Hospital and with the results reported by the workers from Rockefeller Institute.[4] In all these studies, Streptococcus haemolyticus pneumonia ranks second in prevalence, averaging about 3 per cent of the total series.

Age and Sex Distribution.—The most important fact brought out in this connection was that the average age in this series of 560 pavillion patients was 45 years, whereas the average age in our Bellevue studies was only 38 years. The sexes were about equally represented, in contrast to studies made in city hospitals, in which the males have far outnumbered the females. In the present study 53.6 per cent were males and 46.4 per cent females. In the Bellevue Hospital studies 83.1 per cent were males and 16.9 per cent females.

Incidence of the Various Types of Pneumococcic Pneumonia.—Table 2 shows the incidence of the dominant types of pneumococcic pneumonia. Type III pneumonia was the most prevalent (20.2 per cent). In

From the Medical Department of the Cornell University Medical College.

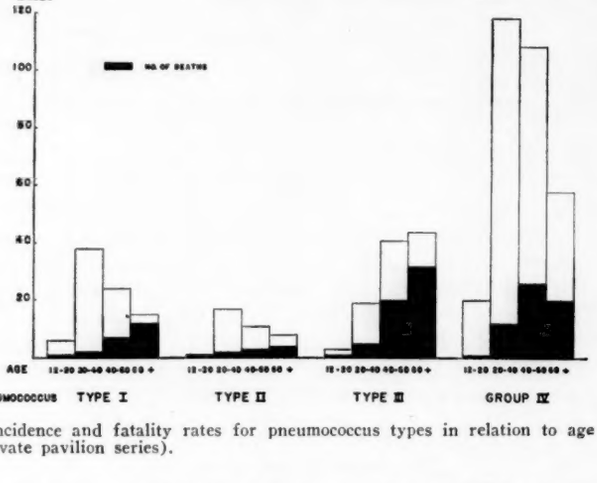
1. Osler, Sir William: The Principles and Practice of Medicine, ed. 1, New York, D. Appleton & Co., 1910.

2. The attending physicians at the hospitals mentioned gave us access to the records of private patients.

3. Cecil, R. L.; Baldwin, H. S., and Larsen, N. P.: Lobar Pneumonia, Arch. Int. Med. **40**: 253-280 (Sept.) 1927.

4. Avery, O. T.; Chickering, H. T.; Cole, Rufus, and Dochez, A. R.: Acute Lobar Pneumonia, Monograph 7, Rockefeller Institute for Medical Research, Oct. 16, 1917.

this respect the present series differs sharply from previous studies, in which type I has been the commonest type. This difference in type distribution can be explained at least in part by the higher age incidence of pneumonia in private patients. The studies by Cecil and his co-workers [5] at Bellevue Hospital showed clearly that the incidence of type III pneumonia increases with age, an observation which has been corroborated by Blake [6] and others.



Incidence and fatality rates for pneumococcus types in relation to age (private pavilion series).

In table 2 one also notes a very high incidence of the miscellaneous types (57.3 per cent), much higher than in most of the series reported from other institutions. Whether this was actually the case or whether the typing was inaccurate it is impossible to say. The newer types have not been separately listed in table 2, as they were recognized only during the last few years of the period covered by the study.

TABLE 1.—*Bacteriologic Classification of 560 Cases of Pneumonia from Private Pavilions*

Bacteria	Number of Cases	Incidence, per Cent
Pneumococcus (all types)	531	94.8
Streptococcus haemolyticus	19	3.4
Streptococcus viridans	2	0.35
Bacillus influenzae	1	0.2
Staphylococcus aureus	4	0.7
Staphylococcus albus	1	0.2
Friedländer's bacillus	2	0.35
Total	560	100.00

TABLE 2.—*Incidence of Pneumococcus Types in Private Pavilion Series*

Type of Pneumococcus	Cases	Incidence, per Cent
Pneumococcus type I	83	15.6
Pneumococcus type II	37	6.9
Pneumococcus type III	107	20.2
Miscellaneous types (group IV)	304	57.3
Total	531	100.0

It is noteworthy that 78.4 per cent of the cases of type II pneumonia occurred in the male and only 21.6 per cent in the female.

In 531 cases of pneumococcic pneumonia in private pavilions, the incidence of type I was highest between the ages of 20 and 40; of type III, after the age of 60, in contrast to the Bellevue figures, which show that the highest incidence of type I occurred between the ages of 20 and 30, and of type III between 30 and 50.

Clinical Characteristics.—The various forms of pneumonia showed the characteristics that have been described in previous studies. Cases due to pneumococci of types I, II and III were nearly always typical lobar infections with classic history, frank physical signs and rusty sputum. The seriously ill patients usually showed signs of multilobar involvement. The "miscellaneous" types often presented an atypical picture, with only partial consolidation of the lobes and purulent rather than bloody or rusty sputum. The patients with streptococcic or staphylococcic infections were, almost without exception, seriously ill but with indefinite signs in the chest.

Bacteremia.—Unfortunately, blood cultures were not taken as a routine in this group of patients. However, 287 patients were subjected to blood cultures, and the results are shown in table 3.

Approximately 24 per cent of the patients in this series yielded positive blood cultures, and in the septic cases the fatality rate was 74 per cent. Patients with negative blood cultures showed a fatality rate of only 16 per cent. However, the figure was unusually high (42.6 per cent) for forty-seven patients with type III pneumonia with sterile blood cultures.

TABLE 3.—*Blood Cultures in the Pneumococcus Series*

Type of Pneumococcus	Positive Blood Cultures			Negative Blood Cultures		
	Number	Deaths	Fatality, per Cent	Number	Deaths	Fatality, per Cent
Type I	12	8	66.7	38	5	13.2
Type II	4	3	75.0	19	1	5.3
Type III	26	21	80.8	47	20	42.6
Miscellaneous types	27	19	70.4	114	9	7.9
Total	69	51	74.0	218	35	16.0

Complications.—Analysis of the complications encountered in the series reveals nothing especially noteworthy. Empyema was the most prevalent complication, showing an incidence of 5 per cent in the pneumococcus series and 26.3 per cent in the cases of streptococcic pneumonia. Type I pneumonia showed an empyema incidence rate of 8.7 per cent. Endocarditis, meningitis and pericarditis were rarely reported. Fibrillation developed in quite a number of the older patients and was usually followed by a fatal termination.

Fatality Rates.—We were particularly interested in determining the fatality rate for patients in the private pavilions. Figures for the various types of pneumonia are recorded in table 4. Cases in which specific therapy was given are omitted. The death rate for pneumococcic pneumonia without serum therapy was 30.1 per cent, a figure which is generally looked on as about the standard for type I pneumonia without serum therapy. For example, Heffron's [7] figures on 2,047 cases of type I pneumonia in the United States and Canada in which serum therapy was not given showed a fatality rate of 30 per cent.

The fatality rate for Streptococcus haemolyticus pneumonia (47.4 per cent) approximates closely previous figures in the literature.[8]

5. Cecil, R. L.; Plummer, Norman, and McCall, Marsh: Pneumococcus Type III Pneumonia, Am. J. M. Sc. **191**: 305 (March) 1936.
6. Blake, F. G.: Observations on Pneumococcus Type III Pneumonia, Ann. Int. Med. **5**: 673-686 (Dec.) 1931.
7. Heffron, Roderick: Final Report of the Massachusetts Pneumonia Study and Service 1931-1935, Commonwealth **24**, January-February-March 1937.
8. Bullowa, J. G. M.: Management of the Pneumonias, New York, Oxford Medical Publications, 1937.

The fatality rate for the entire group of 450 cases is 31.7 per cent, which checks pretty closely with the fatality rates for the wards of large city hospitals.

Fatality Rates for Various Pneumococcus Types.—The fatality rates for the dominant types of pneumococcic pneumonia are indicated in table 5 and are compared with similar figures from the series previously

TABLE 4.—*Fatality Rates in Relation to Bacterial Etiology*

Bacteria	Number of Cases	Deaths	Fatality, per Cent
Pneumococcus (no serum)	421	127	30.1
Streptococcus haemolyticus	19	9	47.4
Streptococcus viridans	2	1	50.0
Bacillus influenza	1	0	0.0
Staphylococcus aureus	4	4	100.0
Staphylococcus albus	1	1	100.0
Friedländer bacillus	2	1	50.0
Total	450	142	31.7

TABLE 5.—*Comparison of Fatality Rates Between Private Pavilion Series and Bellevue Hospital Series*

Types of Pneumococcus	Present Series (No Serum)			Bellevue Hospital (No Serum)		
	No. of Cases	Deaths	Mortality, per Cent	No. of Cases	Deaths	Mortality, per Cent
Type I	31	10	32.0	234	73	31.2
Type II	23	7	30.4	441	215	48.8
Type III	102	56	54.9	500	210	42.0
Miscellaneous	265	54	20.4	373	109	29.2
Total	421	127	30.1	1,548	607	39.2

reported by one of us from Bellevue Hospital.[3] The fatality rates for pneumonia at Bellevue Hospital are proverbially high, but it will be seen from table 5 that the rates for our private pavilion series are not so far below them. Indeed, the fatality rate for 102 cases of type III pneumonia in the private pavilion series is considerably higher than that for a similar series at Bellevue.

As in all previous studies, the fatality rate for the various types increases with the age of the patient, as shown in the accompanying chart.

Results with Serum Therapy.—It is interesting to note that in only 60 per cent of type I cases in the private pavilion series was type I serum given. In the type II cases an even smaller proportion was given the benefit of specific therapy. In the newer types it was not to be expected that a high proportion of the patients would receive serum therapy because of the difficulty in many instances of obtaining the serum. However, in view of the well established efficacy of type I serum, it is difficult to understand why so many physicians withheld serum therapy from their type I cases.

Furthermore, the results obtained in fifty-two cases of type I pneumonia in which serum therapy was given were not so favorable as those which have been reported by various observers from large city hospitals such as Bellevue, Harlem[8] and the Boston City Hospital.[9] The reason for the high figure in the present series is easily discovered: In too many cases the serum treatment was initiated quite late in the disease.

Thirty-five patients with type I pneumonia were treated with serum during the first three days of the disease. In this selected group the fatality rate was only 14.3 per cent. In twelve cases of type II pneumonia in which serum therapy was instituted during the first three days there was only one death (8.3 per cent).

It must also be remembered that the average age in this series of patients is almost a decade higher than that reported in studies from various city hospitals. This factor must certainly be considered in comparing the results of serum in the present study with the results obtained elsewhere.

The value of serum therapy for the newer types, especially types V, VII and VIII, has been pretty well established by Bullowa,[10] Finland and Tilghman[11] and others. The results of serum treatment for the new types are well summarized by Lord and Heffron[12] in their recently revised monograph on pneumonia and serum therapy. In the present study the results with serum therapy in these types (table 6) were certainly encouraging, though the number of patients treated was too small to have much significance.

A few of the patients in this series received anti-pneumococcus rabbit serum. The number of patients, however, was not large enough to justify any inferences concerning its relative value as compared with horse serum. It is interesting to compare the total of 107 cases of all types in which serum was given with 221 cases in which none was given. The fatality rate in the group in which serum was given was approximately half of that for the group in which no serum was given (20.5 per cent versus 38.4 per cent).

PATIENTS SEEN IN CONSULTATION

In addition to the 560 cases studied in the private pavilions of hospitals, we have collected from our personal records 351 cases of pneumonia which were seen only in consultation. The data obtained in these cases are naturally not as complete as those derived from the hospital charts of the private pavilion patients.

TABLE 6.—*Results of Serum Therapy in 107 Cases of Pneumonia from Private Pavilion Series*

Types of Pneumococcus	Treated with Serum			Untreated		
	No. of Cases	Deaths	Mortality, per Cent	No. of Cases	Deaths	Mortality, per Cent
Type I	52	12	23.1	31	10	32.0
Type II	14	3	21.4	23	7	30.4
Type III	5	2	40.0	102	56	54.9
Type IV	6	2	33.3	11	0	0.0
Type V	6	1	16.7	7	3	42.9
Type VII	4	0	0.0	12	1	8.3
Type VIII	16	1	6.3	12	2	16.7
Type XIV	2	0	0.0	8	3	37.5
Type XV	0	0	0.0	7	1	14.3
Type XVIII	1	1	100.0	3	0	0.0
Type XIX	1	0	0.0	5	2	40.0
Total	107	22	20.5	221	85	38.4

TABLE 7.—*Varieties of Pneumonia in Consultation Practice*

Organism	No. of Cases	Incidence, per Cent	Deaths	Fatality, per Cent
Pneumococcus (all types)	320	91.1	126	39.4
Streptococcus haemolyticus	20	5.7	10	50.0
Staphylococcus aureus	9	2.6	9	100.0
Tubercle bacillus	2	0.6	2	100.0
Total	351		147	41.9

9. Sutliff, W. D., and Finland, Maxwell: Type I Lobar Pneumonia Treated with Concentrated Pneumococcic Antibody (Felton), J. A. M. A. **96**: 1465 (May 2) 1931.

10. Bullowa, J. G. M., and Greenbaum, Evelyn: Pneumonia Due to Pneumococcus Type VII (Cooper), Arch. Int. Med. **60**: 179-192 (Aug.) 1937.

11. Finland, Maxwell, and Tilghman, R. C.: Clinical and Immunologic Observations in Cases of Pneumococcus Type V Pneumonia Treated with Specific Antibody, New England J. Med. **215**: 1211 (Dec. 24) 1936.

12. Lord, F. T., and Heffron, Roderick: Lobar Pneumonia and Serum Therapy, Commonwealth Fund, 1936.

However, every case seen in consultation was followed up for information concerning termination, complications and the like. Only cases in which the type of bacterial infection was definitely established are included in this group.

Age and Sex Distribution.—In the consultation series the average age and sex distribution was approximately the same as that noted in the private pavilion series.

Distribution by Type.—In table 7 the varieties of pneumonia are shown. The figures differ somewhat from those already presented for patients in private pavilions. In the consultation series the percentage of cases of pneumococcic pneumonia is lower and the incidence of cases of streptococcic and staphylococcic pneumonia is twice as high as in the private pavilion series. This difference was to be expected in a group of serious cases, such as those composing the consultation series.

Incidence of Various Types of Pneumococcic Pneumonia in Consultation Series.—In table 8 it will be noted that the incidence of the prevalent types of pneumococcic pneumonia does not differ widely from that observed in the private pavilion series. Type III and the miscellaneous types compose a large percentage (65.6 per cent) of the group, just as in the private pavilion group.

TABLE 8.—*Incidence and Fatality Rates of Pneumococcic Pneumonia in Consultation Practice (Serum Treated and Non-Serum Treated Combined)*

Type of Pneumococcus	No. of Cases	Incidence, per Cent	Deaths	Mortality, per Cent
Type I	79	24.7	19	24.1
Type II	31	9.7	14	45.2
Type III	74	23.1	44	59.5
Miscellaneous types	136	42.5	49	27.7
Total	320	100.0	126	39.4

TABLE 9.—*Fatality Rates of Consultation Patients Who Received Serum*

Type of Pneumococcus	Received Serum	Died	Per Cent
Type I	63	15	23.8
Type II	27	13	48.1
Type III (rabbit serum)	2	1	50.0
Miscellaneous types	16	5	31.3

Complications.—In this series of consultation cases, most of them severe infections, one would expect a rather high incidence of complications, and such proved to be the case. Empyema occurred in 12.6 per cent of all cases of type I pneumonia, with a death rate of 29.9 per cent, endocarditis in 1.1 per cent and meningitis in 0.85 per cent of all cases. Most of these consultation cases were seen in the home, with the family physician, and it is quite likely that a certain number of complications, such as terminal empyema, endocarditis and meningitis, were overlooked for lack of x-ray and other laboratory facilities.

Fatality Rate.—The case fatality rate for the entire series of consultation cases, including all types, both serum treated and non-serum treated cases, was 41 per cent, a very high rate and one that clearly indicates the serious prognosis in the group under consideration (table 7). In table 8 the case fatality rates for the dominant pneumococcus types are indicated. One is impressed with the high fatality rate for type III pneumonia, 59.5 per cent, which is considerably greater than that for type III pneumonia (40 per cent) in city hospital clinics. Here again we must recall the age of the patients. One of the commonest types of patient encountered in consultation practice is the elderly patient with type III pneumonia, and a very high percentage of them die.

The fatality rate is also very high for the Streptococcus haemolyticus infections (50 per cent) and runs up to 100 per cent in the series of Staphylococcus aureus pneumonia (ten cases).

The fatality rate for patients with positive blood cultures was 70 per cent as compared with 42 per cent for patients with sterile blood cultures. A considerable number of patients with type III pneumonia died without developing sepsis, as in the pavilion series.

Serum Therapy.—Sixty-three patients with type I pneumonia received type I serum (table 9), with a fatality rate of 23.8 per cent, a figure practically identical with that for the serum treated patients in the private pavilion series. This rate is much too high for serum treated type I infections. In most of the large series studied from city hospitals the death rate for serum treated type I pneumonia has varied from 10 to 16 per cent.

The results of serum therapy in this series has been disappointing, chiefly because in nearly all cases the infections were severe to begin with, but more important still because many of these patients received serum late in the disease. For example, the death rate for sixty-three patients with type I infection who received serum was 23.8 per cent, while for sixteen patients who received no serum there was a fatality rate of only 25 per cent. However, for forty patients who received type I serum during the first three days of the disease there was a fatality rate of only 17.5 per cent. An analysis of the cases that were fatal in spite of serum treatment makes it quite obvious in most instances why the patient was not saved by the specific serum. For example, seven patients were treated after the fifth day and one patient was treated as late as the fourteenth day. Two patients had insufficient serum, one receiving only 6,000 units. Two patients died of pulmonary embolism after they had recovered from pneumonia. Two more were elderly alcoholic addicts.

What has been said concerning the type I cases applies equally to the type II series (table 9). The serum treatment again made a poor showing in a small group of cases. The number of cases of the higher types in which specific serum therapy was used is too small to be significant.

COMMENT

This study has provided a considerable amount of information concerning pneumonia in private practice. Of prime importance is the fact that the social stratum of the patient has little to do with the prognosis, which depends not so much on the economic status of the person as on his age, on the type of pneumonia and, most important of all, on the availability and early use of serum. With regard to the cost of antipneumococcus serum, its efficacy has now been so clearly proved that it should be supplied free by state and city boards of health, as is the case, for example, in the city and state of New York. It would appear from Rogers' figures that the death rate for pneumonia is lowest among patients who receive treatment at home. We imagine that the same will be found to be true in a similar study now being made by the health department in the city of New York.

One should not infer from this, however, that patients receive better treatment at home than they do in the private pavilions of hospitals. Nor should the inference be made that transportation in an ambulance is a detriment to the patient's chance of recovery. The Rockefeller Institute's statistics on pneumonia have always been among the best; yet practically every patient in their records was admitted by ambulance. The most plausible explanation is that the practitioner sends his sick patients to the hospital but allows his patients with mild attacks to remain at home. Certainly this seems the most rational explanation of the difference in death rates between home and hospital cases. At this point one may well raise the question of the proper disposition of the pneumonia patient in private practice. Should he be treated at home or should he be transferred to a convenient hospital? In answer to this question, several factors have to be taken into consideration:

1. Has the patient a comfortable home with proper facilities for handling the sick?
2. Does the patient live in town and at a convenient distance from the doctor's office or does he live in the country where he is inaccessible to emergency care?
3. Is the hospital under consideration provided with a medical house officer who is capable of handling medical emergencies such as vasomotor collapse, cyanosis or pulmonary edema?

There are certain obvious advantages in having a pneumonia patient under hospital care. The most important of these are that a clinical laboratory where sputum and blood cultures can be frequently examined is accessible; x-ray examinations are conveniently made; a house officer is usually available to handle any emergency that develops; oxygen therapy can be more readily supervised; serum treatment can be given at regular intervals, a procedure which is difficult to carry out in the private home, and, finally, if a surgical emergency arises, treatment can be promptly initiated.

Several facts brought out by this study are worthy of further comment. The fact should be stressed that the average age incidence of pneumonia among the well-to-do classes is almost a decade higher than that of pneumonia in the wards of large city hospitals. Pneumonia at Bellevue Hospital is a disease of young working men; pneumonia in private practice is a disease of the middle aged and elderly.

Certainly one of the most interesting facts elucidated has been the very high incidence and death rate of patients in private practice with type III pneumonia. Type III pneumonia, by reason of its prevalence and fatality rate of almost 60 per cent, has come to be one of the most serious problems that the practitioner has to face. It is made doubly serious by reason of the apparent failure of type III serum to control the infection.

It was disappointing to find so many histories of private patients with pneumonia in the hospital files with no record of any bacteriologic study. However, this investigation covers a period of ten years. During the last five years, sputum typing and blood cultures have been carried out in a much higher percentage of cases. This applies also to the use of antipneumococcus serum in the treatment of type I pneumonia. Only 60 per cent of the patients with type I pneumonia in the private pavilion series received type I serum. However, the percentage of cases in which serum therapy was used is definitely higher for the last five years of the study than for the first five years. With respect to the series of 351 cases of pneumonia in the consultation series, the fact should be stressed that we are dealing here with a group of very ill patients. The fatality rate in this group was quite high for every type. The lesson to be derived from a study of this group is that consultations should be held early in the disease, when special therapy such as oxygen and serum will be of most value to the patient.

Pneumonia in private practice is not so mild a disease as it has often been considered to be. Certainly in New York private hospital pavilions the fatality rate is surprisingly high—no doubt definitely higher than the rate for small towns and rural districts.

We regret that we cannot speak with more authority concerning the value of serum in the treatment of the newer types of pneumonia. Our impressions have been quite favorable, particularly in the serum treatment of types V, VII and VIII, but the number of cases observed is too small to have statistical value.

We have omitted statistical data on the dosage of serum administered, since accurate details were not always available from the patient's chart. In nearly every case the serum employed has been of the concentrated and refined type of horse serum first described by Felton. The new method of giving serum in large single intravenous doses of from 100,000 to 150,000 units seems to have no deleterious effects when given very slowly, but we agree with Lord and Heffron that it is still wiser for the general practitioner to administer serum in frequent divided doses.

Only fifteen patients in our entire series were treated with antipneumococcus rabbit serum. Because of the small number of cases in this group, we have refrained from drawing any conclusions. However, apart from the fact that rabbit serum is available for some types for which there is at present no horse serum (types VI, XVII, XVIII and so on) we have found no noteworthy difference either in the course of the disease or in the incidence of complications when compared with those treated with refined horse serum. In a patient with type III pneumonia who received approximately 850,000 units of concentrated type III rabbit serum early in the disease there developed, several days after administration of serum, a pneumococcus type III empyema necessitating resection of a rib.

SUMMARY

1. Nine hundred and eleven cases of pneumonia from the records of private practice were reviewed with special reference to the incidence and fatality rates for the various types and the results of serum therapy.

2. The data obtained from the "private practice" series were compared with well established data based on pneumonia records from the public wards of large city hospitals.

3. The most significant facts brought out by this comparative study are:

(*a*) The generally higher age incidence of pneumonia in the well-to-do classes.

(*b*) The high incidence of type III pneumonia in private practice. This probably results in part from the higher age incidence of this group.

(*c*) Inadequate bacteriologic study of the "private pavilion" cases. Less than half of the patients available for study had been properly typed.

4. Only 60 per cent of the private pavilion patients with pneumococcus type I infections received type I serum. In the "consultation series" a much higher proportion received serum. The results of serum therapy in both series were not as favorable as those obtained

in the general wards of large city hospitals; the fatality rate of 23.5 per cent for the entire series of 115 cases of type I pneumonia in which serum therapy was given is almost double that reported from various other sources and is not conspicuously lower than the standard fatality rate (30 per cent) for type I non-serum treated cases. A number of factors, such as the higher age incidence, the severity of the cases studied, delay in administering serum, or inadequate dosage are probably responsible for this high figure.

5. Pneumonia in private practice is not so mild as it has often been claimed to be. In view of the well demonstrated value of specific therapy in pneumonia, administration of serum should be part of the routine treatment in every case amenable to such therapy, regardless of the social status of the patient.

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THE TOXEMIAS OF PREGNANCY

TREATMENT BASED ON A NEW CONCEPT OF THE ETIOLOGY

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A new concept of the physiology and pathology underlying the development of the toxemic state in pregnancy is based on old and new knowledge of the role of body fluids in maintaining the integrity of the organism. A method of treatment is derived from this concept in the light of facts developed in connection with studies on water balance, acid-base equilibrium, renal function and shifts in body water and electrolyte.

Newburgh [1] and his associates have measured water exchange in many persons with normal and abnormal renal function. They found that if the intake of water was restricted in cases of impaired renal function, retention of urinary solids would result. If large amounts of water were given, the quantity of urinary solids excreted would be comparable to the excretion by a normal person ingesting the same diet. From these data they were able to calculate the amount of urinary water necessary to remove definite quantities of urinary solids. As the concentrating ability of the kidneys lessened, more urinary water was necessary to remove the urinary solids.

Fluid is held within the body in two main chambers, the extracellular and the intracellular compartment. The cells of the body are surrounded by interstitial fluid. This fluid carries nourishment to, and waste away from, the cells. It also controls the temperature of the organism and maintains osmotic equilibrium and a stable hydrogen ion concentration.

The fluid contained in an organism amounts to approximately 70 per cent of the body weight. The extracellular fluid accounts for 20 per cent and the intracellular for 50 per cent. The extracellular fluid is composed of the blood plasma 5 per cent and the interstitial fluid, including lymph, 15 per cent of the body weight. In a person weighing 150 pounds (68 Kg.) the body fluid would be distributed approximately as in table 1.

Darrow and Yannet [2] found that when there was an increase in extracellular electrolyte there was a shift of body water from the cells to the extracellular fluid but that when there was a decrease in extracellular electrolyte there was a shift of water from the extracellular fluid into the cells. They pointed out that, as nine tenths of the osmotic pressure of body fluids is maintained by electrolyte, the shift of body water is largely governed by the distribution of electrolyte.

When urinary solids are retained there is an accumulation of both urinary waste and electrolyte in the blood plasma. It then becomes necessary for the organism to make adjustments to maintain osmotic equilibrium and to keep the hydrogen ion concentration within normal limits if normal metabolic activity is to persist. Small molecules and inorganic ions pass readily across the capillary membrane into the interstitial spaces. The interstitial fluid, in order to maintain osmotic equilibrium with the intracellular fluid, draws water from the cells. Darrow and Yannet [2] emphasized the fact that, when the concentration of electrolyte in the extracellular fluid is altered, serious symptoms can follow the shift of body water from the cells to the extracellular fluid even though the total body water is unchanged.

Gamble [3] pointed out that in considering electrolyte one deals not with salts but with separately controlled concentrations of anions and cations. Therefore when retention of urinary solids is present a consideration of the food ingested is of great importance. The average diet composed of liberal quantities of milk, fruits and vegetables yields a basic ash. If when retention occurs the diet ingested yields a basic ash, there will be an increase of base in the blood plasma. Ordinarily the kidneys control the amount of base in the blood, but if renal function is hampered and excess base is not eliminated the excess base must move out of the blood plasma into the interstitial fluid to preserve a normal hydrogen ion concentration. This shift produces edema, or swelling, of the interstitial spaces, and shrinking, or dehydration, in the cells.

If the diet yields an acid ash and the excess ions cannot be excreted, the lungs will dispose of carbonic acid, thus keeping acid and base in balance. Clinical edema will not be noted. This protective mechanism alters the composition of the blood plasma, and gradually an important buffer, bicarbonate, is depleted and replaced by acid ions which should have been excreted. A serious toxemia, with no appreciable edema, may develop.

Newburgh [4] has developed a diet the ash of which gives a neutral reaction. By using this diet he is able to supply ample food without disturbing the delicate acid-base balance.

THE TOXEMIAS

It is believed that toxemia will not develop if no impairment of renal function exists. The impairment may be so slight that no test yet developed will point

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1. (*a*) Newburgh, L. H.; Wiley, F. H., and Lashmet, F. H.: A Method for the Determination of Heat Production Over Long Periods of Time, J. Clin. Investigation **10**: 703-721 (Oct.) 1931. (*b*) Wiley, F. H., and Newburgh, L. H.: An Improved Method for Determination of Water Balance, J. Clin. Investigation **10**: 723-731 (Oct.) 1931. (*c*) Lashmet, F. H., and Newburgh, L. H.: A Comparative Study of Excretion of Water and Solids by Normal and Abnormal Kidneys, ibid. **11**: 1003-1009 (Sept.) 1932. (*d*) Newburgh, L. H., and Lashmet, F. H.: The Importance of Dealing Quantitatively with Water in the Study of Disease, Am. J. M. Sc. **186**: 461-471 (Oct.) 1933.

2. Darrow, D. C., and Yannet, Herman: The Changes in the Distribution of Body Water Accompanying Increase and Decrease in Extracellular Electrolyte, J. Clin. Investigation **14**: 266-275 (March) 1935.

3. Gamble, J. L.: Extracellular Fluid, Bull. Johns Hopkins Hosp. **61**: 151-173 (Sept.) 1937.

4. Newburgh, L. H., and MacKinnon, Frances: The Practice of Dietetics, New York, MacMillan Company, 1934, chapters 11 and 13.

it out. However, when the burden of fetal excretion is added without a sufficient increase in fluid intake there may be a retention of urinary waste and electrolyte. As the blood plasma is not able to rid itself of these retained products it becomes hypertonic. In order that osmotic equilibrium may be retained there must then be a shift of water from the reservoir of the body, the intracellular compartment. This shift of water will at first aid in the excretion of some of the retained solids; but, as the retention increases, some of the small molecules and inorganic ions will pass into the interstitial spaces. More water is then drawn from the cells to maintain osmotic equilibrium with the surrounding fluid.

The changes within the body will be influenced by the reaction of the residue after the food is burned. A diet yielding an alkaline ash will produce a shift of water from the cells to the interstitial spaces. The result is cellular dehydration and edema. If the diet yields an acid ash, water will be drawn from the cells to increase the urinary output. The result is an increased concentration in the intracellular and extracellular fluid. In both instances metabolic activity is altered by increased concentration within the cells.

TREATMENT OF THE TOXEMIAS OF PREGNANCY

Newburgh [1c] demonstrated that impaired kidneys could be made to excrete the normal amount of urinary solids if large amounts of fluid were ingested. Treatment of the toxemic patient must vary for the nonconvulsive and the convulsive type, yet the basic principle remains the same. To overcome the retention of urinary solids large quantities of fluid must be ingested. As fluids are taken liberally the blood plasma becomes hypotonic. In other words, the osmotic pressure of the blood plasma is less than that of the interstitial spaces. As a result, water will pass to the interstitial fluid and small molecules and inorganic ions will pass into the blood plasma. The interstitial fluid, then maintaining osmotic equilibrium with the intracellular fluid, gives up water to the cells and the cells are hydrated.

A great deal can be done to prevent the toxemias of pregnancy. Newburgh [1c] has found that impaired kidneys do not produce a highly concentrated urine even though the intake of water is restricted. Dieckmann [5] reported the mean for the maximum specific gravity in normal pregnancy to be 1.022. A patient not ingesting a great deal of fluid and excreting urine having a specific gravity of 1.020 or lower should be considered to have some retention of urinary solids. The presence of renal epithelium in the urinary sediment suggests renal damage.

The treatment of mild toxemia is simple, and progress of the toxemia may be averted. The success of the treatment depends on the cooperation of the patient. Fluids are forced. A urinary output of 2,500 cc. will be ample unless great renal impairment exists. A neutral diet is prescribed. This may be devised from the list of foods prepared by Newburgh.[4] As sodium is a predisposing cause of edema, foods having a low sodium content are chosen, and for the same reason sodium chloride and sodium bicarbonate are eliminated.

Severe nonconvulsive toxemia is treated in a similar manner. The patient should be observed more closely, because of the severity of the symptoms. Hospital care is of great value. The patient with severe preeclampsia may be treated over a long time if large quantities of fluids are given and if the urinary output is correspondingly large. A neutral diet is necessary, as it does not disturb acid base equilibrium.

In the case of the convulsive toxemias, fluids cannot be given by mouth; therefore a parenteral route must be chosen. Fluids are more rapidly absorbed when given intravenously, but the subcutaneous method of administration is also valuable. The object is to give large amounts of fluid. Eichelberger and Hastings [6] have demonstrated that hypertonic dextrose solution dehydrates the cells. They found that isotonic dextrose solution would make water available to the cells. Therefore as the cells are already dehydrated and as hypertonic dextrose solution will increase that dehydration, isotonic dextrose solution is given.

The amount of fluid necessary may be determined roughly. Coller and Maddock [7] found that a dehydrated patient had lost 6 per cent of body weight. A convulsive patient weighing 150 pounds (68 Kg.) should have the following needs considered in the first twenty-four hours: water to hydrate the cells, 4,100 cc.; urinary water, 3,000 cc.; vapor water (skin and lungs), 1,000 cc.; total, 8,100 cc. A large estimate must be made for urinary water if the kidneys are to excrete large amounts of retained urinary solids.

TABLE 1.—*Distribution of Body Fluid*

Extracellular fluid		13,600 cc.
Blood plasma	3,400 cc.	
Interstitial fluid	10,200 cc.	
Intracellular fluid		34,000 cc.
Total		47,600 cc.

Very little medication is necessary even though convulsions are present. Usually an initial intramuscular injection of soluble phenobarbital will control the convulsions until intravenous treatment is instituted. It has not been necessary to repeat this medication, as the irritability disappears as fluids are given.

Two thousand cc. of 5 per cent dextrose solution may be given intravenously in about two hours. After 1,000 cc. has been given, the administration of 5 per cent dextrose solution by hypodermoclysis is started. A total of 4,000 cc. of the solution is given in about eight hours. The fluid given subcutaneously is absorbed very rapidly. Diuresis is not expected immediately, as available water will first replace that lost by the dehydrated cells. Within twelve hours it is unusual if a patient will not drink water when encouraged. Water is given freely by mouth, but only water. It is usually necessary to give fluids by the parenteral route for several days before a patient will take enough by mouth.

It is generally true that a patient treated in this manner will regain consciousness before renal excretion is reestablished. It seems logical to deduce that all the cells of the body are in such urgent need of water that many processes are suspended. As the cells are hydrated, those processes are resumed. Convulsive patients are not given food until after three days of freedom from convulsions. They are then treated as patients with severe nonconvulsive toxemia.

5. Dieckmann, W. J.: Renal Function in the Toxemias of Pregnancy, Am. J. Obst. & Gynec. **29**: 472 (April) 1935.

6. Eichelberger, Lillian, and Hastings, A. B.: The Exchange of Salt and Water Between Muscle and Blood, J. Biol. Chem. **118**: 197-204 (March) 1937.

7. Coller, F. A., and Maddock, W. G.: A Study of Dehydration in Humans, Ann. Surg. **102**: 947-960 (Nov.) 1935.

COMMENT

Starling [8] emphasized first in 1896 and later in 1908 the important relationship between disease and the physiology of body fluids and their electrolytes and colloid osmotic pressures. Since that time his theories have been confined by Darrow and Yannet, Gamble, Peters, Landis, Hastings, Eichelberger and others. Starling noted that the important function of the kidneys is to regulate the amount and composition of the total fluid in the body. If by some change in that function the molecular concentration of the fluid surrounding the cells of the body is altered, it is necessary for the cells to give up or take on water until the osmotic pressure within the cell is equal to that of the extracellular fluid.

Newburgh [1c] has demonstrated that a liberal fluid intake is necessary for the proper excretion of urinary solids in persons having impaired renal function. When fetal metabolism increases the normal amount of urinary solids, retention may occur as a result of insufficient urinary water. Because of the great reservoir in the interstitial spaces much of the retained material can immediately be removed from the blood plasma so that osmotic equilibrium is maintained. Studies of the blood chemistry do not then reveal a true picture of the retention process.

TABLE 2.—*Summary of Maternal and Infant Mortality for Toxemias of Pregnancy in Cases in Which the Infant Reached a Period of Viability*

Date	Antepartum Observation	Cases	Infants	Maternal Mortality	Infant Deaths and Stillbirths	Infant Mortality, Percentage
Nonconvulsive, All Types						
1931-1935 1,000 deliveries; treatment conservative	Yes	45	46	0	3	6.5
	Not treated until toxemia was severe	7	8	0	3	37.5
1935-1938 1,000 deliveries; treatment, forced fluids, neutral diet	Yes	53	54	0	1	1.8
	Not treated until toxemia was severe	6	7	0	4	57.0
Convulsive Type						
1931-1935	Yes	2	2	0	0	0
	Not treated until toxemia was severe	4	6	0	2	33.3
1935-1938	Yes	0	0	0	0	0
	Not treated until toxemia was severe	0	0	0	0	0

The treatment then should be based on removing the retained solids from the organism rather than on neutralizing them, or on treating separate symptoms, such as edema, cerebral manifestations and blood pressure. Large amounts of fluid taken over many days will promote a copious renal output. When the toxemia is of the nonconvulsive type this water may easily be taken by mouth. Most patients will ingest 5,000 cc. a day with only a little encouragement. In order to avoid the ingestion of any excess acid or base, a neutral diet is given.

In treating eclampsia, control of the convulsions is necessary. This control may be obtained by soluble phenobarbital given intramuscularly. As soon as the convulsions are controlled fluids may be given. The intravenous method is the method of choice at first. Eichelberger and Hastings [6] found that hypertonic dextrose solution produces prompt diuresis but dehydrates the cells. It will not produce a permanent urinary output. There is often a depletion of glycogen in the toxic patient, so at first a large amount of dextrose solution may be utilized. So long as that utilization takes place some water will be liberated to overcome cellular dehydration, but little will be accomplished in removing retained urinary solids. Isotonic dextrose solution, on the other hand, liberates large quantities of water when the sugar is burned.

During the development of toxemia, water is withdrawn from the cells to furnish diluent for excess electrolyte and retained solids. The cells then become concentrated. This increased concentration is in osmotic equilibrium with the extracellular fluid, but the concentration produces a pathologic state within the cells. It is well known that an organism can survive with no food for a long period but that when water is restricted life is limited. The vital part of the organism, the cells, becomes dehydrated under conditions which draw water from the intracellular compartment. This process alters cellular function and endangers life.

De Snoo [9] reported unusually excellent results in preventing eclampsia by the use of a salt-free diet and fluids. He attributed the cause of the convulsion to salt rather than to a physicochemical change in the relationship between the blood plasma, the interstitial fluid and the intracellular fluid. Failure to consider the reaction of the residue of the diet will account for the rare failure of his treatment.

The milk diet has gradually been abandoned by many obstetricians because it apparently instituted convulsions. Milk yields an alkaline ash but, if with each glass of milk one and one-half slices of salt-free bread are ingested, an ideal neutral diet is provided. With this diet many patients may be treated at home without the help of an expert dietitian.

The dehydration therapy of Arnold and Fay has been used successfully by the originators. Over a long time, serious damage to tissues must result unless sufficient water is given to allow the kidneys to excrete all the urinary solids. However, when a dry diet is used as they specify, it must of necessity yield an acid ash. This diet would be of great value for a patient having gross edema, as much of the edema fluid would be liberated to provide sodium ions to maintain a normal hydrogen ion concentration. For patients having no edema and other signs of toxemia, the treatment is dangerous.

The action of magnesium sulfate is not known. Stander [10] found in experimental work that magnesium sulfate produced moderate necrosis in the central part of the lobule of the liver and moderate degeneration in the convoluted tubules of the kidneys. As serious damage to the liver and kidneys may result from the

8. Starling, E. H.: The Herter Lectures on the Fluids of the Body, Chicago, W. T. Keener & Co., 1909.

9. de Snoo, K.: The Prevention of Eclampsia, Am. J. Obst. & Gynec. **34**: 911-939 (Dec.) 1937.

10. Stander, H. J.: Effect of Intravenous Administration of Magnesium Sulfate, Tr. Sec. Obst., Gynec. & Abd. Surg., A. M. A., 1928, pp. 210-224.

toxemia alone, it seems unwise to use a drug which may increase the damage. It is possible that magnesium sulfate may be most valuable by furnishing the acid SO_4 ion.

Most low protein salt-free diets are unsuccessful because the ash is strongly basic. If the diet was designed to yield a neutral ash it would be satisfactory.

Recently great emphasis has been placed on plasma proteins. Darrow and Yannet found that electrolyte accounted for about 90 per cent of the osmotic pressure exerted by body fluids. They also found that when electrolyte was increased the plasma proteins decreased. When the extracellular fluid is made hypertonic by retained urinary solids and electrolyte, water is drawn from the cells to maintain osmotic equilibrium between the intracellular and the extracellular fluid. The extracellular fluid is diluted by the additional water and the plasma proteins will be relatively decreased. It is not easy to increase the plasma proteins by diet, but they may be increased by removing excess electrolyte, by the ingestion of large amounts of water.

By following the treatment outlined it is possible to treat patients having considerable tissue damage, provided enough water is ingested to allow impaired kidneys to excrete retained urinary solids. It must constantly be borne in mind that the cells will be dehydrated to some extent when edema exists. Therefore a successful treatment should point first toward hydrating the cells and second toward promoting urinary excretion. The fact that coma disappears before urinary excretion becomes normal when fluids are given freely suggests that cellular dehydration has an important role in the pathologic process of the toxemias of pregnancy.

This treatment will control the development of severe toxemia, making it unnecessary to induce labor in a seriously toxic patient until after the toxemia is under control. The maternal risk is greatly decreased, and in addition the fetal mortality is lessened. The modern tendency to induce labor as toxemia becomes more severe leads to a low maternal mortality, but many babies are lost as a result of fetal toxemia and prematurity. A successful method of treating the toxemias of pregnancy should be productive of a low fetal mortality as well as a low maternal mortality.

The result of treating the toxemias in 2,000 consecutive deliveries is presented in table 2. The toxic patients were divided into two groups. The group seen for the first time with severe toxemia was eliminated as having had no antepartum care. In most instances fetal heart tones were not heard when the patient was admitted; therefore treatment had no bearing on the fetal mortality.

In the group receiving antepartum care an interesting comparison is possible. One thousand patients were delivered between Aug. 1, 1931, and June 1, 1935. Forty-five had a nonconvulsive toxemia. The fetal mortality was 6.5 per cent. Two patients had eclampsia. Only one convulsion was recorded for each patient. The treatment in this group was conservative. Fluids were given in moderate amounts, and the diet was low in protein and salt. No attention was paid to the reaction of the diet, and it consequently yielded a basic ash. Labor was induced if the toxemia became more severe.

A second group of 1,000 patients was delivered between June 1, 1935, and March 20, 1938. Fifty-three had a nonconvulsive toxemia. There were no convulsive patients. The treatment was as outlined in this paper. Fluids were forced, and a neutral diet low in sodium was given. The fifty-three mothers were delivered of fifty-four babies. One baby, a fetal monstrosity, was lost, so that the fetal mortality was 1.8 per cent.

SUMMARY

1. The toxemias of pregnancy occur in women with some previous impairment of renal function. This impairment leads to a gradual retention of urinary waste and electrolyte.

2. Retention of urinary solids leads to dehydration of all the cells of the body and the fetus. Dehydration alters the function of the cells and accounts for metabolic changes in the various organs of the body.

3. Retention of electrolyte is responsible for the different types of toxemias. A diet yielding an alkaline ash leads to retention of alkaline ions and the development of cellular dehydration in the presence of edema. A diet high in acid ash leads to retention of acid ions with general dehydration of all cells.

4. The toxemias may be prevented by the ingestion of large quantities of fluid and a neutral diet low in sodium if treated early, or they may be controlled at any time if treated before severe cellular damage has resulted.

5. The infant mortality for the toxemias of pregnancy can be lowered.

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ABSTRACT OF DISCUSSION

DR. P. J. CARTER, New Orleans: Dr. McPhail's paper is in keeping with the present day treatment of the toxemias of pregnancy. I agree that urinary solids should never be allowed to be retained on account of the accumulation of urinary waste and electrolyte in the blood plasma, as a result of impaired renal function. An attempt to secure a neutral ash is important, for if renal function is hampered a disturbance in water balance may occur with a resulting toxemia. The mechanism by which water is displaced or added to in a toxic individual and the reaction of the tissues and cells to such a toxemia are excellently outlined in Dr. McPhail's paper. The effect on the kidney shows the most striking abnormalities in toxemia; it is believed that toxemia will not develop when no impairment of renal function exists. The adage "dehydrate in edema" has well stood the test, and the proper use of the tonic solutions of dextrose has been our greatest accomplishment in lessening the maternal and fetal mortality in the toxemia of pregnancy. In our present knowledge of cell activity whereby little or no edema occurs when water becomes bound up in the cell protoplasm, as against visible edema when the fluid accumulates in the intracellular spaces, we have an important factor influencing water balance. I cannot agree with Dr. McPhail in giving 2,000 cc. of 5 per cent dextrose solution intravenously in about two hours, with a total of about 4,000 cc. in about eight hours. This seems to me an excessive amount of water to give a patient in eclampsia, in which the heart action has been disturbed and disabled, and this amount would tend to cripple its action still further. My observations through the Charity Hospital at New Orleans, where we have an abundance of material, have been that eclamptic patients fare better with a lesser amount of concentrated solution at longer intervals; namely, 500 cc. of a 20 per cent solution intravenously every six hours or even in a greater concentration in the individual case. In the toxemias of pregnancy we are still treating the symptoms of a disease of little known origin, but which reveals to us a disturbed water balance in which an excessive intake or ouput results in the accumulation in the intracellular spaces of water producing edema, or accumulating in the cells with little or no edema. In summing up, the salt element and its concomitant reactions with retention and storage of chlorides play a most important part in the development of pregnancy toxemia. One cannot begin to attain a proper water balance and a proper ratio in osmotic pressure, which are essential in the treatment

of this disease, when one loads the overburdened tissues and cells with additional water and excess of electrolyte.

DR. LYLE G. MCNEILE, Los Angeles: I congratulate Dr. McPhail in presenting a new concept of the etiology of the toxemias of pregnancy and the development of a treatment based on a new concept. Any theory, however, must establish beyond question the premises on which it is based. It appears to me that in order for Dr. McPhail to establish his case he must either assume or prove certain facts. First he must prove that there is renal impairment in all cases of toxemia. Delicate clearance tests of kidney function in the toxemias have frequently failed to disclose such impairment. Secondly he must demonstrate that the degree of renal impairment must be sufficient to cause a retention of electrolytes (sodium, potassium, chloride and the like as well as urinary solids). In the early stages of eclampsia there almost always is no impairment of the concentrating power or of the ability of the kidneys to excrete electrolytes. The concentration of the urine during the phase of acute oliguria is usually over 1.030. Page, in my clinic, has made numerous Addis tests of concentrating power in selected cases of severe eclamptogenic toxemias and has failed to obtain specific gravities of less than 1.026 on any of them after from eighteen to twenty-four hours of dehydration. The work of Newburgh and others quoted by Dr. McPhail refers only to the amount of water required to excrete urinary solids when there is a known impairment of concentrating powers of the kidney. Dieckmann, Killian and Stander, moreover, have found that the concentration of electrolytes in the blood of eclamptic patients is within the normal range. The author answers this in his paper by stating that blood chemical studies do not always reveal "a true picture of the retention process." As affecting certain phases this may be true, but in the matter under discussion it is hardly true, for the electrolytes are freely permeable through capillaries and are in constant equilibrium between the blood and extracellular fluids. Thirdly the proponent of this theory must show that such a retention of electrolytes would lead to a "cell dehydration" without producing general dehydration. Darrow and Yannet state that the loss of electrolytes produces the symptoms and signs of dehydration but that an increase of extracellular electrolytes experimentally leads only to the symptom of extreme thirst. I have never noted such pathologic thirst as a symptom of toxemia. Is it true that the blood in eclampsia becomes hypertonic? Harden and his associates, Seitz, and the authors of the first paper on our program seem to have demonstrated that the blood may become hypotonic through loss of albumin in the urine. This would lead to cell hydration rather than cell dehydration. Most important, a proponent of this theory must show that cell dehydration would lead to a suspension of cell function or to any of the symptoms of eclampsia.

DR. FRANCIS L. MCPHAIL, Great Falls, Mont.: Darrow and Yannet noted dry mucous membranes and increased thirst in animals after increasing the extracellular electrolyte. In experiments a large amount of salt was injected into small animals. When a retention process develops in pregnancy it develops slowly and the extracellular electrolyte is probably increased to a lesser degree. Nevertheless the mucous membranes appear dry in many toxic patients. If 500 cc. of 20 per cent solution of dextrose is given, very little water will pass into the cells. While glycogen depletion is present in the toxemic state, a concentrated solution of dextrose may be utilized, but as glycogen is replaced in the tissues only a small amount of dextrose is oxidized and little water is liberated to hydrate the cells. A method of treatment has been presented which has worked well in the prevention and treatment of eclampsia and in the treatment of severe nonconvulsive toxemias. It does not depend on polypharmacy. Adequate renal excretion and restoration of function have resulted. The value of the treatment may be determined after a fair trial.

Duration of Life in Sixteenth Century.—In the sixteenth century the average duration of life was eighteen years. Fully one-half the population of every country died under the age of twelve, and 60 per cent of those died before their fifth year.—Hurd-Mead, Kate Campbell: A History of Women in Medicine, Haddam, Conn., the Haddam Press, 1938.

RELATION BETWEEN BLOOD PLASMA PROTEINS AND TOXEMIAS OF PREGNANCY

A PRELIMINARY REPORT

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MONTGOMERY, ALA.
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Diets for pregnant women are not modern, though their use in the past was more empiric than scientific. The angel in Biblical times gave the father of Samson instructions before his birth, saying "She may not eat of anything that cometh from the vine, neither let her drink wine or strong drink nor eat any unclean things" (Judges 13: 14). Since then each generation has added or subtracted, restricted or insisted, on a variety of foods. The textbooks of the middle nineteenth century have practically no antepartum advice and only mention that an adequate diet should be prescribed for convulsions without saying what constitutes an adequate diet.[1] Even as late as 1928 De Lee,[2] in his antepartum instructions concerning diet, did not advocate a balanced diet. He advised that the patient "omit meats and broths and limit eggs and fish." Curtis,[3] with two full pages on diet, said "Meat is to be taken moderately." This is an advance toward balancing the diet. Beck,[4] however, hewed to the conventional diet of the past—the decreasing of proteins during the latter part of pregnancy and the restricting of proteins in the case of toxemia, the animal proteins being replaced with vegetable proteins.

Several years ago it became evident to one of us that certain patients in the antepartum clinic of the City Memorial Hospital of Winston-Salem, N. C., who had edema or high blood pressure seemed to improve clinically even though they continued to eat meats when instructed to abstain. As this was before an increase of protein in the diet was beginning to be advocated, it was thought best to stress a salt-free and porkless diet, omitting the restriction of other proteins but urging, as before, that more milk be taken. Many patients volunteered the information that they ate beef and eggs, and these were not restricted in amount. With this diet there were no cases of eclampsia in the clinic in four years, though previously there had been several cases each year.

During a conference with Strauss in Boston in 1936 we mentioned the fact that, while we did not advocate the use of proteins during the latter part of pregnancy or in cases of toxemia, we did not restrict them and our patients were consuming varying amounts with no apparent harm. Strauss at this time was studying the effect of very high protein diets on toxemia, diets with 260 Gm. of protein daily, in the form of milk, lean meats and egg whites. His patients lost weight, their blood pressure fell, the subjective symptoms abated and

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Mr. Walter Mickle cooperated in the laboratory determinations.
Read before the Section on Obstetrics and Gynecology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

1. Meigs, Charles D.: Treatise on Obstetrics: The Science and Art, ed. 2, Philadelphia, Lea & Blanchard, 1852.
2. De Lee, Joseph B.: Principles and Practice of Obstetrics, ed. 5, Philadelphia, W. B. Saunders Company, 1928.
3. Curtis, A. H.: Obstetrics and Gynecology, Philadelphia, W. B. Saunders Company, 1933.
4. Beck, A. C.: Obstetrical Practice, Baltimore, Williams & Wilkins Company, 1935.

in some cases the albuminuria was decreased. These had been the effects, to a lesser degree, with some of our patients when they had taken protein against our instructions. We planned to give some of our clinic patients an increased protein intake, as a routine, to see how they would react. Because of the low economic status of our patients and our lack of hospital beds for experimental work we arbitrarily decided on six whole eggs a day in addition to the 1 or 2 quarts of skim milk and the legumes which they might have. They were told to eat whatever meat they had, aside from salt pork. Knowing that an increase of protein was against previous training, we did not feel it wise to omit the magnesium sulfate when indicated and insisted that they use a salt-free diet. Most of the patients reported that they felt so much better and a few of the toxemias improved so dramatically that it became a routine to have the patients add six or eight whole eggs to their daily diet. One of the first patients given this diet was a Negro girl aged 14, seen in one of our rural antepartum clinics. She was eight months pregnant, had a blood pressure of 190 systolic, 110 diastolic, a 2 plus reaction for albumin, and edema, with headache and dizziness, and appeared very stupid. She was put on the old routine of a low protein diet, with from 2 to 3 quarts of skim milk daily, rest in bed and magnesium sulfate. At the next clinic, two weeks later, she had gained 10 pounds (4 Kg.), appeared more stupid and had a blood pressure of 200/115. Both the mother and the nurse who had seen her during the past two weeks assured us that she had followed instructions. We added from eight to ten whole eggs to the milk, thus giving her around 90 Gm. of protein a day. The family lived in the country and had enough eggs for her. When seen two weeks later she had lost 10 pounds, was very clear mentally and had a blood pressure of 140/90 and no albuminuria. She was delivered spontaneously before her next clinic visit, without any evidence of toxemia appearing during or after labor.

It was about this time that Harden's [5] monograph was brought to our attention. In his cases he attempted to maintain a positive balance of nitrogen in order to supply the fetal requirements without depleting the maternal proteins. He calculated the amount of protein required in the cases of toxemia by adding to the minimum amount required for maintenance 50 Gm., the amount of protein metabolized, as evidenced by the end products in the urine and the estimated requirements of a 2 kilogram fetus. His patients averaged from 75 to 80 Gm. of protein daily. Though we had chosen our amounts arbitrarily, we found that we had been giving approximately the same amounts as Harden. In a four year series he [6] found that none of the 522 patients given his protein stabilization diet had had convulsions, while the frequency of convulsions in referred cases in the locality remained the same. Our experience has been similar, as will be shown.

Our empirically chosen amounts of protein and the calculated amounts of Harden were considerably less than the amounts given by Strauss. While our clinic patients were having no eclampsia, some were having toxemia, though it was milder in those who were able to obtain the milk and eggs. Were the toxemias of our patients who subsisted on turnip greens, sweet potatoes and corn bread, with occasionally fresh fish and pork, due to a lack of protein or to an improperly balanced diet, which needed a positive balance of other nutritive factors required by the fetus? We determined to estimate the blood plasma proteins of a series of patients who were receiving the type of diet which they would have had if they had not been pregnant or had had no instructions in diet to see whether there was a significant change in plasma proteins. These patients were instructed to eat and live as they had before they knew that they were pregnant. As we had previously been urging them to increase the proteins by adding milk, eggs and cheese to the diet and to cut down the salt intake, we did not begin to collect the specimens of blood until after they had been on their new diet for at least a week. They were told to take no magnesium sulfate and to eat the same amount of salt they usually did, as well as to prepare the food with seasoning meat.

The plasma proteins of the blood of thirty-four nonpregnant women of the same social status from the clinic were used as controls.

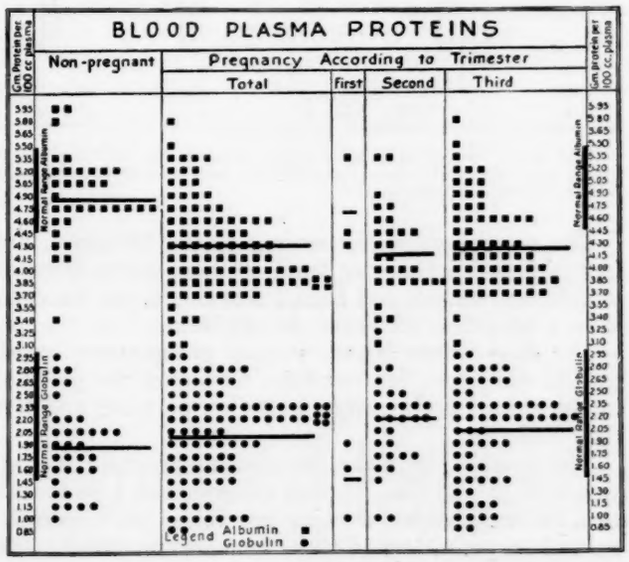

Chart 1.—Plasma albumin and globulin concentrations for thirty-four nonpregnant women of the same economic status as the pregnant women, for the pregnant women as a group and for the pregnant women by trimester. In the charts each square and circle represents one determination, and the horizontal lines represent the average values for each group. (See text for probable error of means.)

Persons who have worked with clinic patients realize that they cannot be controlled like guinea pigs in cages. However, in choosing the patients for this study we tried to make sure that those classified as having a normal pregnancy or receiving a regular diet were not getting a high protein intake. Some of the patients in this group should probably be included in the high protein group, as we had a feeling that they were eating more protein than they would admit. This is easy to understand, because, having been on an adequate protein diet previously, they did not feel as well with a restricted protein intake. As a result of this our figures may be somewhat higher than they ought to be, particularly for the third trimester.

The albumin and globulin were determined by the method of Bowman. It was thought well to divide the pregnant patients according to the three trimesters and to group together those who we were certain were on a high protein diet and those who had toxemia. The patients with toxemia all had a blood pressure of 145/100 or higher and were known to have had a nor-

5. Harden, Boyd: A Study in Pre-Eclampsia and Eclampsia, Pittsburgh, University of Pittsburgh, 1936.
6. Harden, Boyd: Clinical Management of Pre-Eclampsia and Eclampsia, Pennsylvania M. J. 40: 835-837 (July) 1931.

mal blood pressure early in pregnancy. Ninety-seven determinations were made for the pregnant women. Three cases occurred in the first trimester, thirty in the second and sixty-four in the third. Twelve of the patients were on a high protein diet, and forty-two were on the regular diet. Eight had definite toxemia.

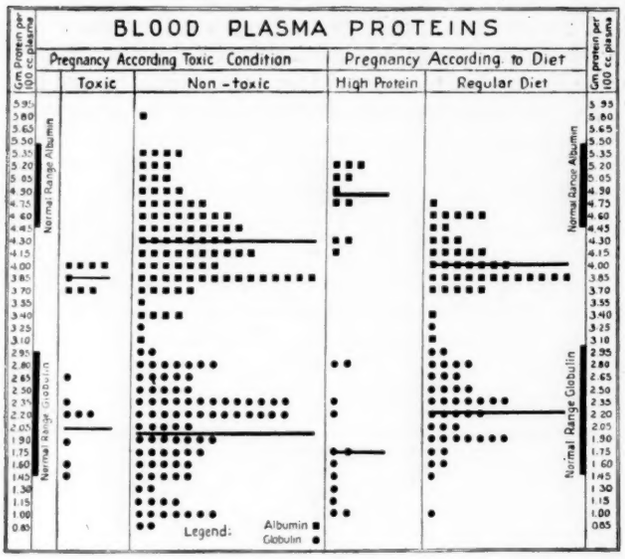

Chart 2.—Plasma albumin and globulin concentrations for the pregnant women in relation to (1) toxic condition, (2) nontoxic condition, (3) high protein diet and (4) regular diet.

The normal values, according to the literature, are from 4.5 to 5.5 Gm. per hundred cubic centimeters of plasma for albumin and from 1.5 to 3 Gm. per hundred cubic centimeters of plasma for globulin.

The class values for the various groups were scaled to 0.15 divisions; for example, all values for globulin in the class 1.6 Gm. were 1.52 Gm. or more and less than 1.67 Gm.

The average, or mean, for the nonpregnant women was 4.90 ± 0.06 Gm. for the albumin and 1.88 ± 0.06 Gm. for the globulin, showing low values but within the normal range. Most of these patients were of the low economic group, who eat only small amounts of meat and milk and few eggs.

The pregnant women as a whole showed a lower mean value than the nonpregnant women, the mean for albumin being 4.27 ± 0.04 Gm. and for globulin 2.01 ± 0.04 Gm. The mean values for albumin for the first trimester, 4.70 ± 0.18 Gm., were higher than those for the pregnant women as a group but lower than the mean for the nonpregnant women. The number of women in the first trimester was very small because most clinic patients do not come to the clinic before the fourth month. The mean value for globulin for this group was lower than that for all the pregnant women, being 1.5 ± 0.14 Gm. There was very little difference in the mean values for albumin for the second and third trimesters, but the values for both were lower than for the first trimester or the nonpregnant women, being 4.18 ± 0.06 Gm. and 4.30 ± 0.05 Gm., respectively. The mean values for globulin for the second and third trimesters were 2.11 ± 0.06 Gm. and 1.99 ± 0.05 Gm., respectively.

The values for patients with toxemia showed a definite lowering of the albumin to 3.87 ± 0.03 Gm. but a rise in globulin to 2.07 ± 0.09 Gm. The change in albumin is in agreement with the experience of Strauss and others. The rise in globulin is a new observation and should be verified. It may be in the nature of a compensatory rise. For the patients receiving a high protein diet, the values were very close to those for the controls; namely, 4.90 ± 0.09 Gm. for albumin and 1.76 ± 0.12 Gm. for globulin, the globulin average being slightly lower than that for the control patients. None of the patients receiving a high protein diet showed any evidence of toxemia, and subjectively they felt very well. Their urine and their blood pressure remained normal. The values for the patients receiving the regular diet were lower than those for the nonpregnant women, being 4.04 ± 0.04 Gm. for albumin and 2.25 ± 0.05 Gm. for globulin.

Chart 3 shows four representative cases. The first two patients had normal blood pressure and weight gain with no toxic symptoms:

CASE 1.—D. E., a Negro primipara aged 17, seven months pregnant, was told to forget her pregnancy and to eat as she pleased. This was her first pregnancy, and she had had no dietary instructions previously. The plasma albumin content dropped gradually from 4.13 to 3.84 Gm. as the globulin rose from 2.12 to 2.28 Gm.

CASE 2.—E. H., a Negro tertipara aged 21, eight months pregnant, was told to follow her regular diet but after two weeks admitted that she had been adding eggs and milk because they made her feel better. We insisted that she refrain from taking the proteins, and on the subsequent two visits she assured us that she was eating as she did when not pregnant.

The next two cases illustrate the effect of the change in diet:

CASE 3.—R. S., a Negro sextipara aged 32, six months pregnant, was changed from her regular diet to one high in protein, containing from 70 to 80 Gm. a day. The albumin rose from 3.98 to 5.07 Gm. and the globulin fell from 2.79 to 1.71 Gm. She had had no complaints or symptoms previous to the change in diet. The next month there was a drop in the albumin and globulin.

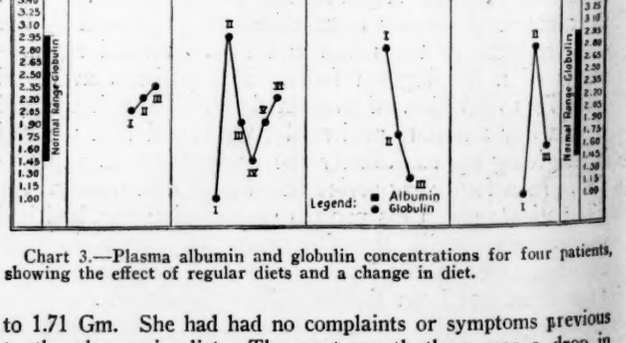
SELECTED REPRESENTATIVE CASES
Blood Pressure and Weight within Normal Limits
No Toxic Signs or Symptoms
Effect of Change in Diet
Gm. Protein per 100 cc. Plasma
D.E. Col. Age 17 Para I 7 months
I. 7-10-37 Regular diet
II. 7-31-37 Regular diet
III 9-4-37 Regular diet
E.H. Col. Age 21 Para III 8 months
I. 6-26-37
II. 7-3-37 On regular diet 2 wks.
III. 7-10-37 Regular diet
IV. 7-17-37 Voluntary addition of eggs & milk
V. 7-24-37 Regular diet
VI. 7-31-37 Regular diet
R.S. Col. Age 32 Para VI 6 months
I. 7-31-37 Regular diet
II. 9-18-37 High protein for two wks.
III. 10-9-37
L.M.B. Col. Age 17 Para 7 months
I 6-26-37 On high protein, changed to regular diet
II On regular diet
III. 7-17-37 Refused to stay on regular diet.
Normal Range Albumin
Normal Range Globulin
Legend: Albumin
Globulin

Chart 3.—Plasma albumin and globulin concentrations for four patients, showing the effect of regular diets and a change in diet.

CASE 4.—L. M. B., a Negro primipara aged 17, seven months pregnant, had been receiving a high protein diet for two or three weeks and was told to return to her old way of eating. One week later the albumin had fallen from 5.30 to 4.23 Gm. and the globulin had risen from 0.83 to 2.37 Gm. She refused to remain on her old diet and had been increasing the amount of milk and eggs. At this time the albumin had risen to 4.67 Gm. and the globulin had fallen to 1.65 Gm.

As has previously been stated, the rise in the globulin with the lowering of the albumin in the plasma is apparently a new observation and should be verified.

COMMENT

Rosenstein [7] more than sixty years ago advanced the theory that cerebral edema caused eclampsia and that edema was due to the effusion of serum from the "too watery" blood into the cerebral tissues. Thirteen years later Charpentier [8] agreed with others that a diminished amount of albumin in the blood was a predisposing cause in the production of eclampsia. Wieloch [9] in 1925 reported the universal occurrence of water retention in his cases of toxemia of pregnancy. Bingham [10] found that toxemia developed in his patients only with excessive gain in weight. The cause of edema in toxemia has been attributed to many things: excessive production of the pituitary antidiuretic hormone,[11] primary kidney disease,[12] instability of the plasma colloids,[13] pressure on the ureter of the enlarged uterus [14] and excess of sodium chloride.[15] In 1937 Strauss [16] observed that patients with hypoproteinemia had a significant gain in weight, with visible edema, rises in blood pressure and in a few cases albuminuria, when sodium was administered as chloride or bicarbonate.

Strauss [17] found that in cases of toxemia with or without convulsions the plasma albumin is lower than that of pregnant women receiving an average diet. The average level of the globulin in his cases was not lower than that of pregnant women receiving an average or low protein diet. The average level of plasma albumin for all our pregnant women was higher than that of his patients. Those of our patients who had signs of toxemia had an average level higher than that of Strauss's patients. The average level of globulin in our cases was lower than in Strauss's cases except in those of toxemia, in which it was slightly higher.

As yet there does not seem to be a clearly defined cause for the lowering of the plasma proteins during pregnancy. It has long been recognized that the fetus is a parasite, drawing from the maternal organism the necessary nourishment for its development and growth regardless of the depletion of the mother's tissues. It is known that calcium will be removed from the body when the blood does not contain a sufficient amount to supply the needs of the fetus. Proteins are essential for growth and repair of body tissue in the adult and certainly are required in considerable amounts by the fetus and its membranes. It would seem necessary for the mother to supply by her diet sufficient proteins to maintain her own growth and repair and supply the needs of the fetus if she is not to deplete her own tissues. That there is a definite decrease in the plasma protein can be seen by our figures, which corroborate those of other authors. As has already been noted, there is considerable variation in the amount of protein which is considered to be adequate in normal pregnancy and in toxemias. The League of Nations Technical Commission of the Health Committee on Nutrition [18] recommended for normal pregnant women from 1.5 to 2 Gm. of protein daily for each kilogram of body weight, which would mean from 70 to 130 Gm. a day for the woman of 150 pounds (68 Kg.); this is a little higher than the intake advised by Harden [5] in cases of toxemia but considerably less than that used by Strauss [17] in his cases. The revised report of this committee [19] stated, in listing the protein requirements of pregnant women, that "some animal protein is essential and in the growing period should form a large proportion of the total protein." The daily amount of protein after the fourth month of pregnancy recommended in this report is 1.5 Gm. per kilogram of body weight.

SUMMARY

1. In pregnant women the blood plasma albumin is decreased below the level found in nonpregnant women.

2. Toxemias of pregnancy uncomplicated by organic disease are associated with a significant decrease of plasma albumin and a questionable increase of the globulin. The increase of the globulin needs further investigation.

3. Pregnancy without signs of toxemia and a diet deficient in protein cause a decrease in plasma albumin.

4. An increased intake of protein in cases of mild toxemia causes an alleviation of objective and subjective symptoms and signs and is well tolerated by the patient.

ABSTRACT OF DISCUSSION

DR. THOMAS ADDIS, San Francisco: The authors of the paper are conservative when they say that they do not think a "clearly defined cause for the lowering of the plasma proteins in pregnancy" has been demonstrated. Their own observations as well as other clinical and experimental data show that the principal and necessary cause is a protein intake that is too low relatively to the greatly increased need for protein during pregnancy. My associates and I have completed experiments in which we compared the total body protein and organ protein of two groups of rats of identical original body weights, one a control group of female rats and the other a group in late pregnancy. We found that in all parts of the body the concentration of protein was less in the pregnant than in the control group and that the greatest change occurred in the blood serum, where the protein content fell from 6.7 per cent to 5.4 per cent. The cause of this change is given by the observation that the pregnant group were obliged to allocate 10 per cent of all the protein in their bodies for the construction of the embryos and uterus and had to use in addition 5 per cent of their total protein for new construction that the pregnancy made necessary. The mothers did their best to meet this requirement by eating more food. But the protein concentration was too low. Even though they ate 50 per cent more than the controls they could not get enough protein. Their gastrointestinal capacity was the limiting factor. As a consequence, they fell into a protein deficit, and the debt was paid at the expense of the mothers for the benefit of the babies. Drs. Dodge and Frost will agree that the need for more protein in the diet continues beyond pregnancy and throughout lactation. We are finding that in rats a diet that is entirely adequate for growth fails to maintain the usual protein content of the mothers' organs and tissues during lactation. The practical importance of these observations of Drs. Dodge and Frost is unquestioned. They give direct evidence that diets sufficient under ordinary conditions for maintenance are grossly inadequate in protein concentration during pregnancy. If we are to exclude the gastrointestinal tract as a limiting factor, it is not enough to give plenty of all sorts of food. We must see that pregnant and lactating women are given food with a high proportion of meat, fish, milk and eggs. From an economic point

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8. Charpentier, L. A. A.: A Practical Treatise on Obstetrics, New York, William Wood & Co., 1887, vol. 2.
9. Wieloch, J.: Arch. f. Gynäk. **123**: 337, 1925.
10. Bingham, A. W.: Am. J. Obst. & Gynec. **23**: 38 (Jan.) 1932.
11. Anselmino, K. J., and Hoffman, Friedrich: Arch. f. Gynäk. **147**: 652 (Dec.) 1931.
12. FitzGibbon, G.: J. Obst. & Gynec. Brit. Emp. **29**: 402, 1922.
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16. Strauss, M. B.: Am. J. M. Sc. **194**: 772-783 (Dec.) 1937.
17. Strauss, M. B.: Am. J. M. Sc. **190**: 811 (Dec.) 1935.
18. League of Nations Technical Commission of the Health Committee in Nutrition, 1935.
19. League of Nations Technical Commission of the Health Committee: The Problem of Nutrition, 1936, vol. 2, p. 15.

of view this may sometimes be difficult, but that it is a strict requirement from the point of view of physiology and of medicine there can be no doubt.

DR. BOYD HARDEN, Burlington, N. C.: I wish to make one point concerning nitrogen deficits in the toxemias of pregnancy. The discussion is based on the premise that there is a physiologic optimum beyond which the administration of protein may accomplish no benefit; there is a pathologic minimum below which the restriction of this vital constitutional element must result in manifestations of deficit. Further, in severe hepatic disease the selection of proteins essential in growth and development is necessary to the pattern needs of the fetus and the storage demands of the maternal host. This study represents a period of seven years during which 739 consecutive admissions with late gestational toxemia and eclampsia were studied under a regimen designated as protein stabilization. Nineteen patients with typical manifestations in preeclampsia and a like number with eclampsia have been selected for this discussion. During the seven years, no patient with well defined preeclampsia developed eclampsia under the regimen of protein stabilization, while the incidence of eclampsia in the community remained the same that it was before the institution of this regimen. The application of the usual methods of antepartum care and the compensation of nitrogen deficits have proved life saving in our hands in preeclampsia and eclampsia.

Study of Nineteen Preeclamptic and Nineteen Eclamptic Patients

PREECLAMPTIC PATIENTS

Average Height	Average Weight	Average Age	Average Intake in Grams: Protein	Fat	Carbohydrate
155.49 cm.	80.4 Kg.	33 years	82	61.1	218

On the Du Bois Chart:
155.49 cm. meets 80.4 Kg. at 1.8 square meters.
At 33 years of age the female requires 36.2 calories per square meter of surface area per hour.
1.8 square meters × 36.2 calories × 24 hrs. = 1,563.84.

Dietary values:

Protein	82.0 Gm. × 4 calories per gram		328.00 calories
Fat	61.1 Gm. × 9 calories per gram		549.90 calories
Carbohydrate	218.0 Gm. × 4 calories per gram		872.00 calories
Administered in diet			1,749.90 calories

Urine:

Average total nitrogen	7.60	Protein equivalent	47.50 Gm.
Average nonprotein nitrogen	6.68	Protein equivalent	41.75 Gm.
Protein loss			5.75 Gm.

Feces:

Average total nitrogen	2.20	Protein equivalent	13.75 Gm.

Analysis:

Protein administered and consumed	82.00 Gm.
Protein metabolized and lost	61.25 Gm.
Protein stored	20.75 Gm.

This protein storage appears in the presence of a starvation level of excretory products of nitrogen in urine. The actual level of excretory products of nitrogenous metabolism was 0.52 Gm. per kilogram of body weight.

ECLAMPTIC PATIENTS

Average Height	Average Weight	Average Age	Average Intake in Grams: Protein	Fat	Carbohydrate
154.1 cm.	80 Kg.	26.3 years	69.4	61	209

On the Du Bois Chart:
154.1 cm. meets 80 Kg. at 1.8 square meters.
At 26.3 years of age the female requires 36.6 calories per square meter of surface area per hour.
1.8 square meters × 36.6 calories × 24 hours = 1581.12 calories as the basic caloric requirement of the mother.

Dietary values:

Protein	69.4 Gm. × 4 calories per gram		277.60 calories
Fat	61.0 Gm. × 9 calories per gram		549.00 calories
Carbohydrate	209.0 Gm. × 4 calories per gram		836.00 calories
Administered and consumed in diet			1,662.60 calories

Urine:

Average total nitrogen	7.42	Protein equivalent	46.37 Gm.
Average nonprotein nitrogen	6.08	Protein equivalent	38.00 Gm.
Protein loss			8.37 Gm.

Feces:

Average total nitrogen	3.40	Protein equivalent	21.25 Gm.

Analysis:

Proteins administered and consumed	69.4 Gm.
Proteins metabolized and lost	67.6 Gm.
Protein stored	1.8 Gm.

This protein storage appears in the presence of a starvation level of excretory products of nitrogen in urine. The actual level of excretory products of nitrogenous metabolism was 0.425 Gm. per kilogram of body weight.

DR. EVA F. DODGE, Montgomery, Ala.: We felt that we should have a larger number of determinations before drawing final conclusions. The few patients who were given the increased protein diet, particularly the eggs, milk and cheese which we found to be within the reach of our rural clinic patients despite their low economic status, were apparently helped by this diet. A pregnant girl of 13 years who was not included in the case reports had a high blood pressure without any other marked toxic symptoms. The blood pressure did not come down with an adequate protein diet. Labor was induced because of the continued high blood pressure. As her blood pressure was about 200 systolic and 110 diastolic six months after delivery we felt that it was not a protein deficiency which was responsible for the high blood pressure. We feel that the whole egg may have something to do with this problem and are now advocating the use of the whole egg instead of just the whites of the eggs. We realize that during lactation the mother needs protein, but our work was entirely with the antepartum group and we did not go into the postpartum problem.

RADIOSENSITIVITY OF MALIGNANT NEOPLASMS OF THE UTERINE CERVIX

HARRY H. BOWING, M.D.
AND
ROBERT E. FRICKE, M.D.
ROCHESTER, MINN.

Carcinoma of the uterine cervix is radiosensitive. Radiosensitivity means sensitive to radiant energy; specifically it is used to describe certain tumors that are susceptible of being injured or destroyed by radium and roentgen rays. This fact was soon learned by the early workers in the field of radium therapeutics. The disease was among the first malignant tumors observed to be amenable to the rays of radium.

The radiosensitivity of the lesion under consideration is relative, since the degree of injurability or destroyability is dependent on many factors. Apparently some of these factors can be evaluated, at least in a measure or in a limited degree. Ewing said: "The general condition of the patient determines the result of radiation, regardless of nearly all other factors. In fresh subjects in good general health, without anemia or cachexia, the results of radiation are usually prompt and definite, whereas in anemic and cachectic subjects with poor circulation, tumors may fail entirely to respond." Some of these factors can be recognized grossly while others are recognized microscopically. The former lend themselves rather well to recognition and discussion while the latter may be studied only by examination of material which is removed at operation or for biopsy, and by postmortem examination of specimens by skilled pathologists. As a rule, the supply of tissue for microscopic study is very limited, especially when one considers that the response to treatment requires days or weeks and that repeated removal of tissue is necessary. During a course of treatment the removal of representative tissue from time to time for microscopic study and for the evaluation of the results of treatment is considered dangerous or inadvisable.

From the Section on Therapeutic Radiology, the Mayo Clinic.
Read before the Section on Radiology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

The capacity of a given malignant lesion of the cervix to respond to irradiation can be determined by frequent observations during the course of treatment, and the duration of this response can be in a measure determined by the number of three year or five year cures in a group of cases. The data presented in this paper were obtained from our daily experience and from the three year results obtained in a group of 1,491 cases in which treatment was given in the years 1915 to 1929 inclusive. As a rule the diagnosis can be made from the chief complaint, history, bimanual pelvic examination and inspection of the vaginal cavity, preferably with the patient in the knee-chest position. The removal of small bits of tissue for microscopic study is of value in confirming the clinical diagnosis and in determining the grade of malignancy. Material for biopsy can be obtained with but little, if any, risk. The diagnosis was confirmed by histologic examination in 947 cases; 872 of the 947 patients were traced after they left the clinic; 372, or 42.7 per cent of these patients, lived three or more years after the treatment. In the entire series of 1,371 traced patients 473, or 34.5 per cent, lived three or more years after the treatment. In the early years covered by this study a biopsy was an elective procedure, but at the present time it is performed as a matter of routine. The routine performance of biopsy has advanced our knowledge of this dreaded disease. Malignant neoplasms of the uterine cervix consist chiefly of squamous cell epitheliomas, which have a dominant tendency toward the higher grades of malignancy. The remaining small group is made up of adenocarcinomas and a few mixed lesions which contain both of these malignant cellular elements. In the majority of the cases an extensive primary lesion is associated with an inflammatory or degenerative process and the therapeutic management[1] requires special consideration.

From the standpoint of radium therapy it is important to classify the lesions according to the extent of the primary and secondary involvement. The following classification has proved satisfactory: Stage 1 indicates that the primary lesion is limited to the uterine cervix, stage 2 indicates that the primary lesion has extended beyond the original site but the uterus is movable, stage 3 indicates that the primary lesion has extended further than in stage 2 and that the uterus is definitely fixed, stage 4 indicates a "frozen pelvis" with extensive pelvic involvement and the probable presence of local and distant metastasis. The term "modified" is used to describe the stage of involvement in cases in which some type of therapeutic procedure had been employed before the patients came to the Section on Radium Therapy. Modified stage 1 denotes that the active lesion is rather small, while modified stage 4 denotes that a "frozen pelvis" is present.

The radium technic employed at the clinic in the treatment of carcinoma of the uterine cervix may be defined as an intensive, multiple or broken-dose method. This procedure is orderly, flexible and effective. The radium therapist should have at his disposal an assortment of applicators such as universal tubes, various needles and gold (radon) seeds. The treatment factors, that is, the amount of radium, the filtration and the distance, as a rule should remain constant, while the time of application and the interval between applications should be varied to meet the needs of the patient. Nearly all patients are placed in the knee-chest position in order to permit careful inspection and the introduction of applicators without trauma

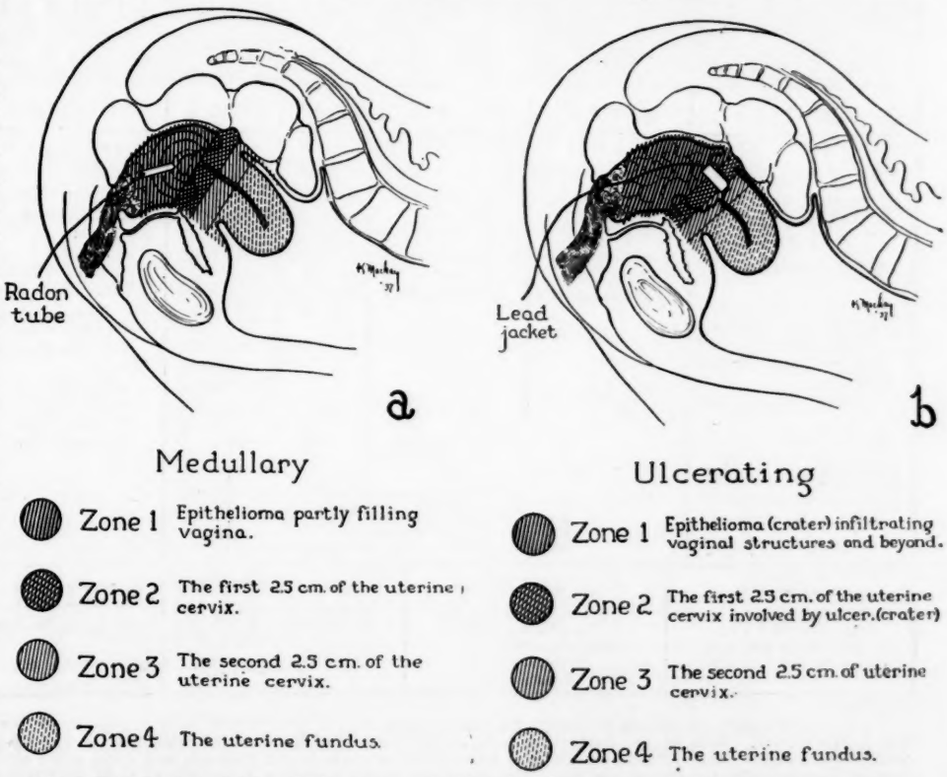
Radon tube
Lead jacket
a
b
Medullary
Zone 1 Epithelioma partly filling vagina.
Zone 2 The first 2.5 cm. of the uterine cervix.
Zone 3 The second 2.5 cm. of the uterine cervix.
Zone 4 The uterine fundus.
Ulcerating
Zone 1 Epithelioma (crater) infiltrating vaginal structures and beyond.
Zone 2 The first 2.5 cm. of the uterine cervix involved by ulcer (crater)
Zone 3 The second 2.5 cm. of uterine cervix.
Zone 4 The uterine fundus.

Fig. 1.—Treatment of (*a*) medullary type, and (*b*) infiltrating types of uterine carcinoma. Patient in knee-chest position and applicator in place.

(fig. 1). The intervals are necessary to determine the radiosensitivity of the treated lesion. In cases in which such complications as tumor necrosis, local cellulitis, ulceration of the vaginal walls that is indicative of potential fistulas, or pyometritis are present the intervals permit the proper institution of active measures to combat these serious, if not dangerous, conditions. In the final part of the course, the treatments are applied more rapidly. The other details are shown in figure 2, in which the probable treatment schedule for an average patient with a stage 3 involvement is outlined. The radium therapy is followed by a course of so-called high voltage roentgen therapy. The combined method of treatment was employed in 1,450 of the 1,491 cases in this series. In the remaining forty-one cases roentgen therapy was the only treatment used.

The classification of the courses of radium treatment is essential for their evaluation. In the event that the

1. Bowing, H. H., and Fricke, R. E.: Carcinoma of the Uterine Cervix: A Survey of Treatment and Results in 1,491 Cases, Am. J. Roentgenol. **40**: 47-51 (July) 1938.

treatment is applied as outlined, together with any additional or probable reduction in the number of applicators, it is classed as complete. In some cases, owing to the character and extent of the local or pelvic involvement, only part of the outline can be carried out. In such cases the treatments are classed as limited. During the course of treatment it may become necessary to stop treatment and in this event the treatment is classed as abandoned. Table 1 shows the most significant factor in estimating the longevity of these patients; 52.9 per cent of the patients who received a complete treatment and 21.4 per cent of those who received only a limited treatment lived three or more years after treatment. This result is all the more significant because in more than 90 per cent of the 1,491 cases the involvement was extensive (stages 3 and 4, table 2). The large number of patients who received limited treatments can be explained as follows. They were treated in the early years covered by this study and when compared with the patients treated in the later years of this study their therapeutic management was considered to be a limited treatment. Of the patients whose treatment was abandoned 30.3 per cent lived three years or more after the treatment (table 1). Much depends on the amount of treatment applied before it is necessary to stop the applications. The analysis of this group is fascinating; many of the patients who lived three or more years after the treatment received a very limited treatment. The associated complications may have been a deciding factor in the response to radium therapy.

We have no statistical data to confirm the statements made about the immediate or initial result. However, the patients who lived three or more years after the treatment may furnish an index. All treatable patients are benefited. The vaginal discharge stops, the tendency to bleed stops, and in many cases the relief of pain is prompt. The degree and the duration of this improvement depend on the extent of malignant involvement and the adequacy with which treatment can be applied.

The patient with stage 1 and modified stage 1 involvement has the best chance of living three or more years after treatment, while the patient who has stage 4 and modified stage 4 involvement has the least chance of living three or more years after treatment. In brief, all treatable patients have a chance of living three or more years after treatment (table 2). An evaluation of these results indicates that the extent of involvement plays a major role in the determination of the longevity of the patient after treatment.

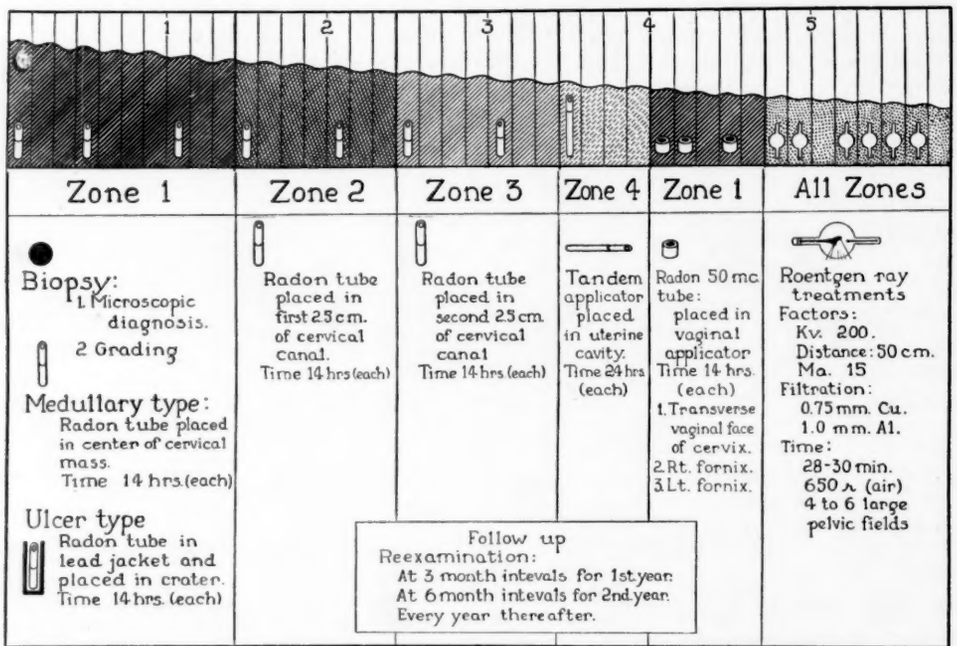

Fig. 2.—Schedule of radium treatment for the average stage 3 involvement in a case of carcinoma of the uterine cervix. Each of the Arabic numerals across the top of the drawing indicates the end of one week of treatment. The vertical line which is intercepted by each Arabic numeral, and every other similar vertical line, indicates the end of one day. The wavy line which descends from left to right indicates the decreasing infiltration and the general improvement of the patient's condition as treatment progresses. Directions for a complete treatment can be obtained by reading the chart from left to right.

Grossly, there are two types of carcinoma of the uterine cervix; these usually are designated as (1) medullary carcinoma and (2) infiltrating or ulcerating carcinoma. The latter type predominates and is more radioresistant than is the former. The grade of malignancy cannot be determined from the gross characteristics of the lesion. However, the gross appearance of the lesion does determine the selection of the type of treatment to be employed in a given case. In other words, the estimation of the grade of malignancy is of but little if any assistance to the radium therapist in determining the treatment to be employed. This statement must be made with a certain amount of reservation because a low grade of malignancy seldom is encountered in cases of carcinoma of the uterine cervix and when it is encountered the neoplasm usually is an adenocarcinoma. It is doubtful whether a squamous cell epithelioma, grade 1, was ever encountered.[2] In other words, our experience centers around the predominating grade 3 and grade 4 lesions. It is evident that if a number of patients who have carcinoma of the cervix are treated individually, irrespective of the grade of malignancy, and if the patients later are grouped according to the grade of malignancy, there will be little difference in the number of three year cures obtained in the various groups. The data in table 3 are submitted to substantiate this statement. Forty per cent of the patients with lesions of grade 1 and 41.1 per cent with lesions of grade 4 lived three or more years after treatment.

Briefly, it seems possible to obtain the same radiotherapeutic result in the treatment of this disease regardless of the grade of malignancy, but one must

2. Broders, A. C.: Personal communication to the authors.

remember that the cases in which the grade of malignancy was low were very few in number and do not warrant a statistical review or opinion. These statistical data warrant further study. We are in accord with MacCarty's statement that one is prone to accept observations too quickly and is likely to draw premature conclusions; this especially is true of microscopic grading and sensitivity.[3]

In order to study the influence of age on the longevity of this group of patients they were grouped according

TABLE 1.—*Results According to the Type of Radium Treatment Employed*

Classification of Radium Treatment	Patients Treated	Patients Traced	Patients Who Lived Three or More Years After Treatment: Number	Patients Who Lived Three or More Years After Treatment: Per Cent of Those Who Were Traced
Complete	604	565	299	52.9
Limited	807	739	158	21.4
Abandoned	39	33	10	30.3
Total	1,450*	1,337	467	34.9

* This does not include forty-one cases in which roentgen therapy was used alone.

TABLE 2.—*Results of Treatment of Carcinoma of the Uterine Cervix with Irradiation Alone, Based on Stage of Lesion*

Stage of Lesion	Patients Treated	Patients Traced	Patients Who Lived Three or More Years After Treatment: Number	Patients Who Lived Three or More Years After Treatment: Per Cent of Those Who Were Traced
Stage 1	13	13	12	92.3
Stage 2	85	81	57	70.4
Stage 3	825	760	292	38.4
Stage 4	156	142	18	12.7
Modified stage 1	4	4	4	100.0
Modified stage 2	28	26	18	69.2
Modified stage 3	297	271	68	25.1
Modified stage 4	83	74	4	5.4
Total	1,491	1,371 (91.9%)	473	34.5

to their ages by decades (table 4). It is an accepted fact that young patients do not tolerate malignant disease as well as do older patients. In other words, the young patient with malignant disease has a poorer prognosis than does an older patient. The data in table 4 substantiate this statement. The number of three year cures of patients treated before the age of 49 years was less than it was of patients treated after the age of 49 years. Patients who were in the fourth and fifth decades of life when radiation therapy was started showed little difference in the percentage of three year cures; however, this statement does not hold true if the patients who were in the third decade of life are included. This may indicate that if it is possible to employ individual treatment for patients in the fourth and fifth decades of life the percentage of three year cures will be approximately the same in the two groups. The percentage of three year cures was increased for patients who were beyond the age of 49 years. It seems probable that age may influence the degree of radiosensitivity but it is possible that the primary lesion responds equally regardless of the age of the patient. However, if metastasis to distant organs occurs before the age of 49 years it may be the factor that reduces the number of three year cures. We do not have data that confirm or disprove this statement.

3. MacCarty, W. C.: Microscopic Grading of Tumors, Its Interpretation, Limitations and Relation to Radiosensitivity, Am. J. Roentgenol. **37**: 365-367 (March) 1937.

A second significant factor occurs in the data contained in table 5. The patients treated early in our experience received a limited radium treatment, for example about 2,000 mg. hours, which may be considered a surface treatment. This was supplemented with the so-called low voltage roentgen therapy and the initial result was favorable; when the patients were seen after an interval of a few weeks, or months, however, activity was demonstrable. As a further palliative procedure the initial treatment was repeated. Many patients received several such treatments but, as a rule, malignant activity was demonstrated on subsequent visits. A careful review of these cases was encouraging but it was evident that the technic was deficient as it did not provide proper distribution of the therapeutic rays of radium, and the initial total dose was too small. For these reasons our present technic was evolved; this accounts in a great measure for the difference in results shown in table 5. Today an initial complete treatment is never repeated and the result is superior when compared with our early results. Of the patients treated between 1915 and 1919 inclusive 14.4 per cent and of the ones treated between 1925 and 1929 inclusive 42.7 per cent lived three or more years after treatment. The radium technic employed today began

TABLE 3.—*Results of Treatment of Carcinoma of the Uterine Cervix with Radiation Therapy, Based on the Grade of Malignant Change*

Grade of Malignancy	Patients Treated	Patients Traced	Patients Who Lived Three or More Years After Treatment: Number	Patients Who Lived Three or More Years After Treatment: Per Cent of Those Who Were Traced
Grade 1	5	5	2	20.0
Grade 2	135	125	56	44.8
Grade 3	407	372	161	43.3
Grade 4	336	311	128	41.1
Biopsy performed but malignancy was not graded	64	59	25	42.4
No biopsy performed	544	499	101	20.2
Total	1,491	1,371 (91.9%)	473	34.5

TABLE 4.—*Results Obtained in the Treatment of Carcinoma of the Uterine Cervix with Irradiation, Based on Age of Patients*

Age of Patient, Years	Patients Treated	Patients Traced	Patients Who Lived Three or More Years After Treatment: Number	Patients Who Lived Three or More Years After Treatment: Per Cent of Those Who Were Traced
20 to 29	28	25	5	20.0
30 to 39	284	266	78	29.3
40 to 49	496	458	145	31.6
50 to 59	452	416	160	38.5
60 to 69	208	185	78	42.2
70 to 79	22	20	6	30.0
80 to 89	1	1	1	100.0
Total	1,491	1,371 (91.9%)	473	34.5

to take form in or about the year 1920. We were favorably impressed with the early results, which encouraged us to persevere and perfect our present plan of treatment.

The hospital mortality was calculated on the basis of the type of treatment applied (table 6). There were 604 complete treatments with one death, a mortality of 0.2 per cent. There were 807 limited treat-

ments with five deaths, a mortality of 0.6 per cent. Every endeavor is made at the time the patient is first seen to select the best type of treatment to meet the therapeutic needs. In other words, every effort is made to avoid, if possible, abandoning treatments. When one considers the numerous applications made throughout the years, the risk attached to a single treatment must be very small; however, the cumulative effect cannot be ruled out. A limited treatment indicates an extensive pelvic involvement and poor general health; it naturally indicates that the risk of treatment would be increased. The hospital mortality in the cases in which the treatment was abandoned was 15.4 per cent. The hospital mortality in the entire series was 0.8 per cent.

SUMMARY

The radiosensitivity of carcinoma of the uterine cervix is a relative feature and its significance must be fully appreciated in the therapeutic management of this disease. If carcinoma of the uterine cervix and the associated inflammatory and degenerative process are effectively treated with radium and supportive measures, the result of treatment is prompt and its duration is evidenced by the percentage of three year cures. An attempt has been made to use the late results as an index of the radiosensitivity of the lesion. Patients possess many potentialities which affect the results of irradiation. The immediate result is influenced definitely by the extent of the malignant process. It is evident that the age and general health of the patient, the equipment and the skill and experience of the therapeutic radiologist have a definite influence on the late result. The best results are obtained in cases in which the treatment is classed as complete at the first session. However, subsequent treatment may produce relief that will last for years. The initial course of radium treatment requiring two, three or more weeks is necessary before one can evaluate the immediate results and determine the radiosensitivity of the lesion. An interval of three months should elapse before one attempts to evaluate the late results. We fully appreciate the limitations of statistical data; however, the data in this paper are supported by our clinical experience.

TABLE 5.—*Results of Radiation Therapy According to Five Year Periods in Which Treatment Was Given*

Five Year Period in Which Treatment Was Given	Patients Treated	Patients Traced	Patients Who Lived Three or More Years After Treatment	
			Number	Per Cent of Those Who Were Traced
1915 to 1919, inclusive..	288	264	38	14.4
1920 to 1924, inclusive..	556	522	185	35.4
1925 to 1929, inclusive..	647	585	250	42.7
Total.....	1,491	1,371 (91.9%)	473	34.5

TABLE 6.—*Hospital Mortality Based on the Classification of Radium Treatment Applied*

Type of Treatment	Patients	Hospital Deaths	
		Number	Per Cent of Those Who Were Traced
Radium:			
Complete.....	604	1	0.2
Limited.....	807	5	0.6
Abandoned.....	39	6	15.4
Roentgen therapy alone*.....	41	0	
Total.....	1,491	12	0.8

* Included in table to account for full total of cases. Not accepted for radium treatment.

ABSTRACT OF DISCUSSION

DR. WILLIAM P. HEALY, New York: About 80 per cent of cancers of the cervix histologically are radiosensitive. Twenty per cent are in the adult group of cancer cells which are relatively radioresistant, but even those cases respond to irradiation because it is only a relative degree of resistance. It is for this reason that cancer of the cervix has gone out of the surgical group into the radiation field of therapy. Rarely is a case of cancer of the cervix encountered in which there is a limited degree of response to irradiation, but occasionally one will meet a case in which improvement occurs for a period of several weeks and the disease is still limited to the cervix and must be grouped as a favorable case clinically, and yet one finds that the cancer does not disappear under irradiation. That patient is incurable under any form of treatment. In this rare instance one is justified in doing a simple, complete hysterectomy, and while the patient lives, which will probably be two or three years, she will remain free from local evidence of cancer. Since all these patients have come for radiation therapy, the degree of radiosensitivity in the individual case is purely of academic interest. One makes a biopsy because one must have a histologic diagnosis in the case, but one is going to treat her with radiation therapy regardless of whether the cancer is of grade 1 or grade 2 and regardless of whether it is a squamous carcinoma or an adenocarcinoma. All cancers do better with radiation therapy in average or expert hands than with surgery. The important item is early diagnosis. If one recognizes these cases early, one has an opportunity of curing 60 per cent of the early group. At the Memorial Hospital we have had 3,500 cases of cancer of the cervix uteri, and we have been impressed by the advantages of giving x-ray therapy with the high voltage x-ray apparatus, 200 kilovolts, before radium is used. It is unfortunate that the authors used only a three year survival classification. That is much too short and is of only academic value, because for cures one must have at least a five year limit. An untreated patient with cancer of the cervix may live two years.

DR. HENRY L. SCHMITZ, Chicago: The paper of Drs. Bowing and Fricke concerns the prognosis and course of the disease in relation to the extent of the growth and the general constitutional condition. The study of the clinical extent of the growth called by the writers stages 1, 2, 3 and 4, either modified or unmodified, would be facilitated if the clinics would agree on the same definitions for each stage. It would then be possible to evaluate the end results of the various forms of treatment of carcinoma of the cervix. The widest differences are found in the definitions of clinical groups 1, 2 and 3. The difference between clinical group 1 and clinical group 2 cases is mobility of the uterus. It is normal in the former if one attaches a forceps to the uterus and it can be displaced down to the entrance of the vagina without causing the patient any distress. In clinical group 2 the uterus is limited in mobility, though movable, and it cannot be displaced downward unless one uses an appreciable pull. Limited mobility may be due to either an extension of the carcinoma or an inflammatory reaction in the pericervical tissues. It is clear that a patient with an inflammatory loss of mobility of tissue will do better than one with a carcinomatous invasion of the paracervicum. The clinical group 3 case is characterized by an invasion of either one or both parametria yet mobility of the entire mass is still present. There should be made a distinction between fixation and limited mobility of the tumor. As soon as the carcinoma becomes fixed, a clinical group 4 carcinoma is present. Presence of local or distant metastases, or invasion of adjacent organs as bladder, vagina or rectum in the absence of fixation, also stamp such a cancer as belonging to clinical group 4. Such a clinical grouping of the extent

of the growth is very important for the selection of the indicated form of treatment and for the study of the good end results. I do not wish to add to these definitions, as the proper grouping alone will enable one to select the treatment and to prognosticate the results.

DR. HENRY ULLMANN, Santa Barbara, Calif.: In the question of clinical stages 1 and 2—and Dr. Schmitz brought up the question of inflammatory reaction—I again want to emphasize, and trust that it will be brought out in the closing discussion again, that quite a number of patients whom I have seen that I would class as a 2, perhaps an early 2 because of a limited mobility, within a few days after a light course of roentgen treatment has been begun, had complete mobility and palpable induration of the immediate part of the broad ligaments. So that a clinical type 2, at first examination, becomes a clinical type 1 after some irradiation. I feel that perhaps we should add to this that a true class 2, type 2, in order to keep our statistics clear, must remain somewhat limited in mobility after a moderate dose of roentgen rays, because I do not believe that this dose will bring back the mobility so promptly unless it is due to inflammation and not to cancer.

DR. HARRY H. BOWING, Rochester, Minn.: Concerning Dr. Healy's discussion a misunderstanding has occurred, as no attempt was made to report the five year results. I did select the three year results obtained in the group of 1,491 cases for comparison to illustrate a few of the many factors that influence radiosensitivity. Briefly, the data on the 1,491 cases were arranged in tables to show the results according to the age of the patient, grade of malignancy (Broders), stage of involvement, the year of the treatment and the type of radium treatment. It is logical to assume that initial or early response to treatment of the primary lesion or, in other words, the radiosensitivity of the lesion, should also be reflected in the three year cures and that it should be possible to measure the duration of this response by an analysis of the three year cures. Naturally, the outstanding single factor governing the early and late results is the stage of the lesion at the time of treatment. In the cases in which the lesion was grade 1, 92.3 per cent of the patients lived three years, but in the cases in which the lesion was grade 4, only 12.7 per cent of the patients lived three years. There was a marked difference in the late result when the calendar year of treatment was tabulated. The technic of radium therapy has improved with the passing of the years. Of the patients treated in the early years of our experience 14.4 per cent lived three years, but of the patients treated in the last five years of this study 42.7 per cent lived three years. Evidently the improvement in technic favored or enhanced radiosensitivity. Adequate radium therapy is not possible in all cases, and as a result patients do not all obtain the same response. In this study 565 traced patients received a complete radium treatment and 52.9 per cent of these patients lived three years. Only a limited radium treatment was possible in 739 of the cases in which the patients could be traced; 21.4 per cent of the patients lived three years. Evidently the adequacy of treatment influences the radiosensitivity. The results according to age groupings are of great interest. The young and old patients are too few for analysis. Of the 458 traced patients who were between the ages of 40 and 49 years, 31.6 per cent lived three years; and of the 416 traced patients between 50 and 59 years of age 38.5 per cent lived three years. Evidently the older patients survive longer than do younger patients or radiosensitivity is influenced by the age of the patient.

Special Institutions for the Insane.—In summing up the movement for special institutions for the insane during the first quarter of the nineteenth century, we find such institutions being established in eight different states for the first time. Of these, six were founded as semipublic institutions by incorporated groups, and two were completely under state auspices. A ninth state, Virginia, established its second state hospital during this period.—Deutsch, Albert: The Mentally Ill in America, New York, Doubleday, Doran & Co., Inc., 1937.

SODIUM CHLORIDE TOLERANCE IN CHRONIC NEPHRITIS

WITH SOME OBSERVATIONS ON THE POTASSIUM AND SULFATE IONS

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AND
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Work published a few years ago [1] on the effect of minerals on fluid balance in experimental nephrotic edema of dogs indicated that sodium entered into the formation of edema, whereas potassium acted to displace it. Further, that the chloride ion was not the active element in the storage of fluid but that it was able to facilitate the formation of edema by uniting with sodium. However, the chloride ion acted as a diuretic by drawing on stored base when administered in excess, such as ammonium chloride, and it was especially effective as a diuretic when given as potassium chloride. This led to a clinical trial of these observations which was found to be effective in many patients suffering with resistant cardiac and nephrotic edemas.[2] The low sodium, high potassium acid ash diet was developed, and 5 Gm. of potassium chloride was added daily for its diuretic effect and for its important assistance as a salt substitute. The past five years have further established the clinical value of this regimen in the control of such problems of edema.

Since in many cases of chronic glomerular nephritis hypertension, cardiac enlargement, gallop rhythm and edema develop late in the disease, a low sodium, high potassium neutral ash diet with potassium chloride was tried. In many instances the regimen was effective in relieving the edema, but too frequently there was a sharp aggravation of the uremic manifestations as an acidosis developed.[3] This led to further specific ion studies on such patients with the hope that additional information of late chronic renal disease might be obtained. Only a few of the observations made on these cases will be presented.

METHOD

Fifteen patients who were faithful to the clinic with long-standing renal disease were sent into the research ward for a period of observation. They were placed on a diet which was found suitable to their taste and to their renal status, so that it could be completely tolerated for many weeks. The diet was then kept constant in nitrogen, phosphorus, sulfur, chloride, sodium and potassium so far as variable sources of individual foods permitted. The problem was carefully explained to the patients so that their complete cooperation was obtained except in one instance. They were kept ambulatory in the ward, sun porches and gardens, which kept them happy.

To this basic program, after a period of observation of from two to four weeks, additions of sodium

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1. Barker, M. H.: Experimental Edema: The Effects of Low Plasma-Protein Level Upon Water Balance as Related to Specific Ions: The Kidney in Health and Disease, Philadelphia, Lea & Febiger, 1935.
2. Barker, M. H.: Edema as Influenced by a Low Ratio of Sodium to Potassium Intake, J. A. M. A. **98**: 2193 (June 18) 1932.
3. Barker, M. H.: Some Dangers of Rapid Diuresis, Illinois M. J. **72**: 313 (Oct.) 1937.

chloride, potassium chloride, sodium citrate, bicarbonate, potassium citrate, calcium gluconate or chloride, phosphoric acid or ammonium sulfate or combinations of these substances were given in amounts calculated for the individual patient. Changes in symptoms, blood pressure, edema, renal function and body chemistries were observed.

Daily weight, fluid intake and output, alternate day or biweekly blood chemical determinations were made

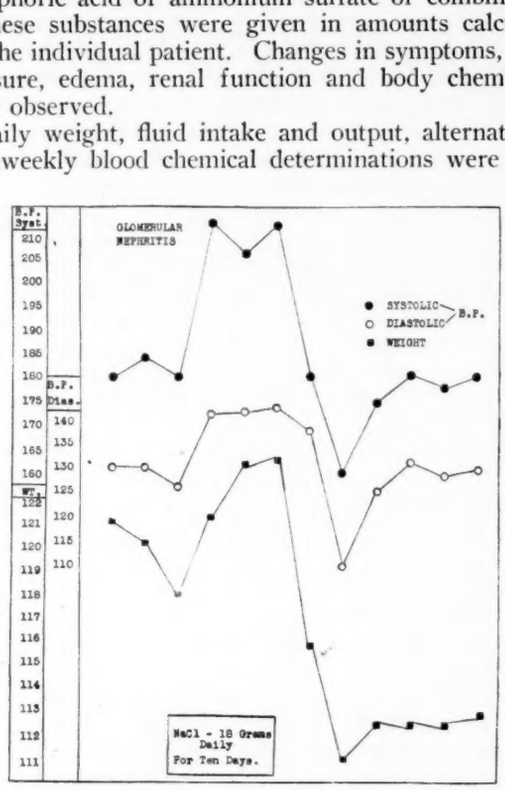

Chart 1.—The systolic and diastolic blood pressures increased sharply when sodium chloride (the equivalent of 2 liters of physiologic solution of sodium chloride) was added to this diet otherwise constant in mineral content.

depending on the acuteness of the case. These observations consisted of the determination of sodium, potassium, calcium, chlorides, phosphates, sulfates, carbon dioxide combining power, urea, urea clearance, creatinine, serum proteins, hematocrit and fluid and blood volumes. Blood counts, phenolsulfonphthalein excretion tests, routine renal function tests, examination of the eyegrounds and chemical studies of edema fluid when present were made weekly as indicated. Blood pressures were taken twice a day.

RESULTS

The chief observations were those of the storage of fluid, aggravation of symptoms, elevation of blood pressure and decreased urea clearance when sodium was added to the basic diet. This was especially true of sodium chloride (chart 1). Chlorides administered as ammonium or calcium chloride or diluted hydrochloric acid frequently decreased the edema, but the associated acidosis aggravated the symptoms and depressed renal function. In certain cases presenting low blood chlorides following the forcing of fluids without a normal intake of chloride or following vomiting the chloride deficit had to be replaced, as Peters and his associates[4] have demonstrated. However, chlorides administered as potassium chloride usually effected a moderate or complete loss of edema and an occasional improvement of urea clearance. There was never a retention of potassium in the cases studied nor was there any evidence of potassium intoxication (chart 2). The administratioin of calcium orally or intravenously did not produce sufficient changes for comment at this time. However, the addition of the acid ions of phosphate and sulfate were of special note. Both ions seemed to be effective occasionally in clearing edema and reducing blood pressure. The former, administered in its most palatable form—phosphoric acid—usually produced a hyperphosphotemia like that seen in acute nephritis or the end stage of chronic nephritis, with a resultant acidosis and aggravation of the renal state. The known seriousness of the storage of phosphorus in renal insufficiency was again clearly shown and the experiment with phosphate was soon discontinued. The sulfate, given as ammonium sulfate, had a much more satisfactory effect. Not only did the blood pressure fall and edema disappear in nine cases but urea clearance improved together with improvement of other subjective symptoms, such as loss of headache, nausea, vomiting and anorexia. Retinal edema and exudate, when present, was relieved. The latter point may be emphasized. Some observations may be more clearly indicated by reference to one of the records of a representative case.

REPORT OF CASE

A. B., a man aged 40, a carpenter, who had acute nephritis in 1931, continued to show urinary changes and a progressive diminution of renal function. Whenever he took salt or salt-containing foods the blood pressure would rise, the urea clearance would fall and edema would form. This state was attended by symptoms of severe headache, pounding of the heart and dyspnea; especially attacks of nocturnal dyspnea were noted whenever the blood pressure would rise over 200 mm. At the time of this study, the urine was acid, the specific gravity was from 1.010 to 1.008 and contained 2 plus albumin, from 4 to 20 red blood cells per high power field and a moderate number of hyaline and granular casts. The phenolsulfonphthalein excretion was 10 per cent and the urea clearance was 30 per cent of normal. There were moderate edema of the face and legs, slight arteriosclerosis and cardiac enlargement. The blood pressure was 160 systolic, 120 diastolic.

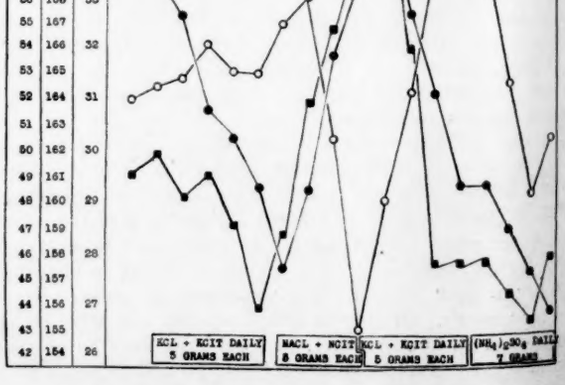

Chart 2.—The administration of the potassium ion as potassium chloride and potassium citrate was associated with a diuresis and an improvement of urea clearance while a sharp depression of the urea clearance and a rapid collection of edema followed an equal amount of sodium chloride and sodium citrate. A return to the potassium salts resulted in diuresis and an improvement of urea clearance.

The diet was kept constant, as already described. Fifteen Gm. of sodium bicarbonate was given daily for two weeks at the beginning of the study as a further check on the sodium ion (chart 3). The chief finding aside from a rapid increase in the carbon dioxide combining power was a depression of the urea clearance until buffering doses of ammonium sulfate

4. Peters, J. P.; Wakeman, A. M., and Lee, Carter: Total Acid-Base Equilibrium of Plasma in Health and Disease, J. Clin. Investigation 6: 517 (Feb.) 1929.

were added. A period of two weeks was allowed for a return to whatever mineral balance this patient was able to regain. At that time 15 Gm. of sodium chloride was taken orally. Very soon there was a sharp decrease in urea clearance and there was a gradual increase both of systolic and of diastolic blood pressure. Symptoms of severe headache, depression, anorexia, heart consciousness, nocturnal dyspnea and stupor gradually developed. By this time the urea clearance had fallen to 10 per cent of normal and the blood pressure had reached 220 systolic, 165 diastolic. A rather dramatic arrest of this trend, followed by an improvement of the urea clearance and a drop

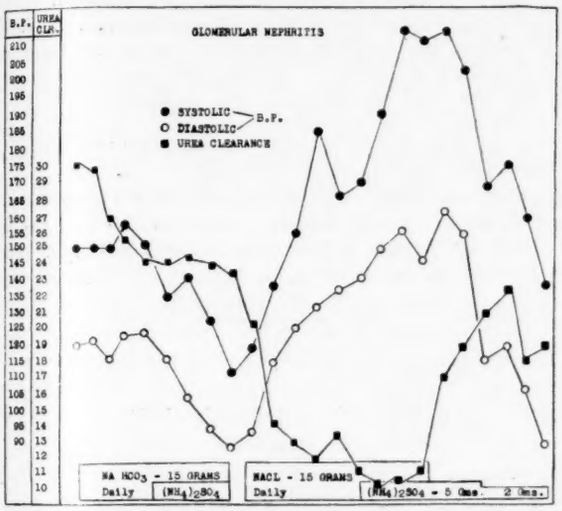

Chart 3.—Sodium bicarbonate administered to a patient with severe glomerular nephritis depressed the urea clearance slightly. When ammonium sulfate was added, the blood pressure decreased, and an arrest of the falling urea clearance was noted. An equal number of grams of sodium chloride substituted for the sodium bicarbonate caused a marked depression of the urea clearance and a sharp elevation of the blood pressure. The addition of a buffering dose of ammonium sulfate seemed to arrest the effect of the sodium chloride.

of the systolic and diastolic blood pressure, was attended by the daily addition of 5 Gm. of ammonium sulfate orally. There was a rapid improvement of all symptoms as soon as the sodium chloride was discontinued. An important sequel to this experiment was the continued symptomatic and clinical improvement attended by the continued administration of the ammonuim sulfate. The patient complained of headache and a general feeling of ill-being, and there was storage of fluid and an increase of the blood pressure when the sulfate ion was discontinued. When the ammonium sulfate was resumed, not only was the patient generally improved but small amounts of salt could be taken on the food without precipitating a renal crisis as that described.

COMMENT

Careful clinical and metabolic studies of fifteen selected cases of advanced renal disease have shown marked elevations of blood pressure, decreases of renal function and associated symptoms in nine cases whenever sodium chloride was ingested. The many sources of sodium chloride in common foods that the salt-hungry patient will naturally select when he is on a salt-free diet renders true restriction of sodium chloride very difficult. Considerable comfort and security may be gained for the occasional patient by giving potassium chloride as a salt substitute, as previously reported. These studies suggest that when one is forced to go on a low protein diet one gives up not only protein but the phosphate and sulfate ions of the meat that play an important role in fluid balance. This factor is no doubt important in the diuretic effect of the high-protein diet frequently given the nephrotic patient. It is further shown that the chronic nephritic patient is readily upset by changes in his mineral intake, apparently because of poor mineral metabolism or clearance. Certainly he is thrown into an acidosis or an alkalosis very easily, either extreme being dangerous. The retention of phosphorus and its effect on acid-base equilibrium with aggravation of the uremic state is emphasized. Further, the possible beneficial effects of the sulfate ion as ammonium sulfate administered in doses of from 2 to 6 Gm. daily was noteworthy in these cases. Although the buffering or neutralizing effect of sodium or some other specific function was not demonstrated in this study, its possible therapeutic value suggests further critical observation. Two patients were unable to clear sulfate readily, and an intoxication and acidosis was noted. The blood sulfates rarely increased over 3 mg., the highest being 7.8 mg. per hundred cubic centimeters. It is obvious, therefore, that although the beneficial effect of ammonium sulfate may be great, its retention must be considered. Since the low protein diet leaves the patient chiefly fruits and vegetables, which supply base in great excess, the need for nontoxic, nonthreshold neutralizing acid elements may be desirable. Ammonium sulfate has been the most helpful of the substances used. Not only is the patient who is required to take a low protein, salt-free diet kept in a better state of urea clearance, circulation and fluid balance, but the addition of ammonium sulfate may permit the taking of small amounts of salt, which renders the diet more palatable. Further, it may cover the sodium chloride, which most certainly will creep into one's food with the disastrous effects demonstrated.

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ABSTRACT OF DISCUSSION

DR. THOMAS ADDIS, San Francisco: This paper is definitely of an experimental nature and so I hope that when the paper is published the authors will make it clear that they are not recommending a low sodium, high potassium diet for all patients with chronic nephritis. It is safe enough for the authors to do it in certain special situations but it wouldn't be safe for the rest of us to use it in all cases. In fact, nothing could be more dangerous than such a diet for patients who are approaching the uremic level, because there one is dealing with a situation in which there is already a strong tendency to lose sodium on account of decrease in renal reabsorption of sodium; and when that is accentuated by any exceptional loss of sodium such as may be produced by vomiting, and it occurs in a patient who is already on a low sodium diet, then unquestionably conditions exist that favor acute renal failure, from which one may save the patient by actually giving him sodium. With respect to a high potassium diet I have a suspicion that in patients who are approaching the uremic level that also may be dangerous. The reason is that I have been making some observations on rats in which an experimental form of uremia had been produced by tying the vena cava. It was found that meat was very toxic to these animals; it increased the mortality. It was natural at first to suppose that this was due to some organic substance associated with the protein in the meat, but further analysis of the situation forced the conclusion that it was really the high potassium content of the meat, not any organic constituent, which was mainly responsible for the increased mortality. And that observation has been verified under altogether different conditions by Dr. Drury at the University of Southern California. Quite independently he came to exactly the same conclusion. I am therefore asking the authors to make it very clear to those who are treating the glomerular nephritis that a low sodium, high potassium diet is no general prescription and that it can be used only under known and highly specific conditions.

DR. WILLIAM DOCK, San Francisco: Dr. Addis has emphasized that when glomerular nephritis begins it does so in an acute form which later ends in uremia and in a few cases in

heart failure. It is in the group having hypertensive heart failure and edema that this diet has been found useful and sodium harmful. When there is vomiting, nausea and finally uremic coma this diet may not be valuable, and in some cases sodium chloride actually seems to be of some use. The point that interested me particularly about this work is that it precedes, or perhaps one might say parallels, some other work that I have been interested in, namely the treatment of hypertension, benign hypertension preferably, by giving the patient an equivalent of Addison's disease. If one can combine a low sodium intake and a high potassium intake, perhaps with salt deprivation, one can produce by giving fairly frequent doses of a mercuric diuretic something equivalent to the Goldblatt hypertensive dog with its adrenals removed. In that state the dog is no longer hypertensive. I hope that the authors will extend their observations to benign hypertension and see to what extent a high potassium, low sodium intake, combined perhaps with further loss of sodium produced by mercurial diuretics, would aid in the control of that particular disorder. Of course, one reason they haven't done this is that his method of treating hypertension with thiocyanate is more effective than most methods that the rest of us have. It is natural therefore that Dr. Barker should be the last to be interested in another way of treating hypertension. In our laboratory we have seen the effect of Dr. Addis's treatment with a low salt diet, a modification of the old French or Allen methods of treating hypertension, which certainly is the most effective form of therapy. As the authors have shown, one must control the diet very rigidly. It isn't enough to tell the patient to stop taking salt. The effect of pushing that therapy to its logical conclusion, in the light of the effect of adrenalectomy on Goldblatt hypertension, should be settled within the near future. A few years ago we might have said "it isn't the hypertension that does the harm, it is the fact this patient has some toxin circulating which gives the hypertension and does the real damage." But the work with the Goldblatt dog shows conclusively that, if the hypertension can be controlled, the whole process will be greatly modified. Since the attack by surgery from the neurologic angle has not been brilliantly successful, other metabolic approaches certainly now seem very inviting.

DR. A. A. HEROLD, Shreveport, La.: The previous speaker talked of the old days of handling nephritis. Twenty years ago I was associated with a man of large experience and good ideas, and in those days the literature was full of the harmful effects of the chlorides in nephritis, and especially with edema. He said to me "It is not the chloride but the sodium radical which is doing the harm" and he suggested to me to use calcium chloride as a substitute for sodium chloride. We found a marked amelioration in the symptoms: toxicity was lower, and the edema almost invariably disappeared by substituting calcium chloride for sodium chloride in the food. That was before the days of the modern substitutes for sodium chloride which now are on the market. But by using small quantities the food was kept from being insipid. The patients got the necessary amount of chloride this way but were deprived of the sodium salt to that extent. While large quantities of the calcium chloride have a bitter taste, a smaller amount cannot be told from sodium chloride. I should like to ask the authors to state whether they have had any experience with the calcium salt and also to tell about their investigation with potassium salts.

DR. M. HERBERT BARKER, Chicago: As Dr. Addis has brought out, it is to be emphasized that this is an experimental observation, but it has definite therapeutic value in the selected case. We selected fifteen cases from a group that had been shown to be particularly sensitive to sodium chloride. No definite reason has been demonstrated for this marked sensitivity. Some individuals with a late chronic glomerular nephritis will show dramatic changes in blood pressure and urea clearance when they get salt, whether by eating anchovies, olives or Hungarian goulash; it doesn't matter where they get it. The chronic nephritic patient does not stand the resulting high blood pressure for any great period of time. We have used potassium chloride considerably, and I know it is dangerous if given fast intravenously or if it is retained in the body. I do not have the fear of potassium that is expressed by some workers. That is probably due to the fact that we have been fortunate in not having potassium intoxication. Clinically potassium chloride has been very well tolerated in the majority of our patients during the last period of ten years during which we have been studying it. Now about the diet in Dr. Addis's rats. I should like to know what the phosphorus level was in the rats that were given meat, because in our work phosphorus was the death-dealing element when protein was administered and not the potassium. As for Dr. Dock's point about low sodium, high potassium in the hypertensive patient, it was immediately suggested when the low potassium, high sodium work came out a few years ago in the treatment of Addison's disease. We have done nothing with this phase of the minerals but it ought to be settled. As to the relation of calcium chloride, we have used it and have not found it notably helpful. We have felt that potassium chloride really entered into the system when chloride was needed and was much more satisfactory than giving the calcium salt, which is broken down in the intestine and the calcium goes out, leaving a free chloride ion which may throw some patients into an acidosis.

TORSION OF THE TESTICLE

JOHN K. ORMOND, M.D.
DETROIT

Torsion of the spermatic cord is now a well established clinical entity, but the individual practitioner meets it so infrequently that in a large proportion of cases it goes unrecognized.

The first authentic report was by Delarsiavue in 1840. In 1936 Abeshouse[1] was able to find 350 instances reported in the literature, which he summarized in a splendid and exhaustive article. The largest individual series were eighteen cases reported by Terazzi and nine cases by O'Conor.[2] To date twelve instances of this condition have come under my observation, two of which have previously been reported.

Although the condition is uncommon, its recognition is of considerable importance, for failure of recognition may result in a testicular atrophy which might have been prevented, and this assumes greater importance in view of the fact that in twenty-four of Abeshouse's 350 cases the condition was bilateral. It is undoubtedly true that in some of the instances of testicular atrophy encountered in the course of routine physical examination the disease is due to previous and usually unrecognized torsion. Atrophy of the testicle is usually due to mumps, trauma (including operation for hydrocele, hernia or varicocele) or torsion. The atrophic testicle of mumps is usually soft and extremely sensitive, while that due to trauma or torsion is firm and insensitive. The undeveloped testis is small and soft but not unduly sensitive.

Torsion has been observed in every decade of life from infancy to old age, though most commonly in adolescence or early adult life. It apparently occurs about as often on one side as on the other, but definitely oftener with maldescent of the testicle than with

From the Henry Ford Hospital.

Read before the Section on Urology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 17, 1938.

1. Abeshouse, B. S.: Torsion of the Spermatic Cord: Report of Three Cases and Review of the Literature, Urol. & Cutan. Rev. **40**: 699 (Oct.) 1936.

2. O'Conor, V. J.: Torsion of the Spermatic Cord: Report of Two Cases and Review of the Literature, Surg., Gynec. & Obst. **29**: 580 (Dec.) 1919; Torsion of the Spermatic Cord, ibid. **57**: 242 (Aug.) 1933.

complete descent. In this connection it is interesting to note that eleven cases of torsion of an intra-abdominal testis are on record.

Two types of torsion are described, intravaginal and extravaginal. Of these the intravaginal type has been observed much oftener than the extravaginal.

In intravaginal torsion the twist in the cord is within the tunica vaginalis and involves the testis and epididymis but not the tunica. Ordinarily the reflection of the parietal layer of the tunica over the epididymis forms a "mesentery" (mesorchium) running from the globus minor to about the middle of the globus major. In many recorded cases this has been much shortened, including only the globus major and hence predisposing to torsion, which may follow slight muscular strain or effort and not necessarily require unusual force.

In extravaginal torsion the twist occurs in the cord outside the tunica and the whole testicular mass is involved. This is often caused by gross violence, though a strong contraction of the cremasteric muscle is said sometimes to cause it.

The first effect of rotation is flattening of the veins and partial obstruction of the venous return; then, as the rotation continues, there occurs obliteration of the veins and finally obliteration of the artery. The effect on the testicle depends on the degree of torsion. If the venous return is not completely obstructed there will be congestion and edema, especially of the epididymis, which is more distensible than the testis. If the venous return is entirely obstructed, congestion is greater and necrosis occurs in a short time. Of course if the twist is sufficient to obliterate the artery prompt infarction occurs.

In some instances, at operation the testicle has been found to be necrotic but no torsion has been demonstrable. In view of the typical character of the attack, it is probable that in these cases torsion had occurred and detorsion had taken place after necrosis had resulted. If detorsion is brought about soon enough necrosis or atrophy may be prevented, though repeated incomplete torsion by causing repeated congestion may eventuate in atrophy.

The majority of cases reported in the literature are of complete strangulation with resultant gangrene. Since the symptoms are severe, operation has often been performed, usually orchidectomy. In some instances, however, detorsion has been possible when the condition was seen early, and there are a few instances of repeated attacks of incomplete torsion with spontaneous detorsion and a smaller number in which attacks of incomplete torsion recurred over a fairly long period and were repeatedly treated by manual detorsion. We have seen these types.

The direction of the twist is not always the same, but O'Conor stated that in the majority of acute attacks the twist has occurred from within outward.

Diagnosis presents some difficulties, especially in the first attack and when, as usually occurs, the patient is seen in one attack only.

The onset is usually sudden and has occurred during sleep, awakening the patient. More often it follows effort or slight and seemingly inadequate trauma, such as that due to diving or bicycle riding. The pain is sharp, its intensity varying with the completeness of the twist. A history of previous similar attacks, clearing up spontaneously, is of extreme importance and almost diagnostic when obtained, and the absence of any history or symptoms of gonorrhea is important.

General symptoms may include nausea, vomiting and occasionally shock. Usually there is no fever, though there may be a slight elevation of temperature. There is usually no leukocytosis.

The urine is generally clear, and urinary symptoms are usually absent. The prostate and seminal vesicles usually present no abnormalities, though there is nothing to prevent torsion from occurring in a man whose prostate is infected.

The affected testicular mass will be found drawn up toward the inguinal region and is usually exquisitely tender, often so tender, in fact, as to prevent satisfactory palpation. Determination of the position of the epididymis is of importance. Normally the epididymis lies posterior and medial to the testis, but in the case of torsion, unless the twist is through 360 degrees or any multiple of 360 degrees the epididymis will be in an abnormal position. The degree of swelling varies and may be great enough to prevent differentiation of the parts of the mass. Therefore the position of the epididymis sometimes cannot be ascertained either because of the swelling or because of the extreme tenderness of the testicular mass. On the other hand, in attacks of recurrent torsion the obstruction to circulation is not complete and the swelling may be confined to the epididymis, making recognition of its position fairly easy.

Elevation of the scrotum is said to accentuate rather than to relieve the pain, as it does in cases of epididymitis, and Prehn called this a characteristic and almost diagnostic sign.

Torsion has been mistaken for acute epididymitis, acute orchitis, strangulated hernia, suppurative inguinal adenitis, acute hematocele and ureteral calculus.

Of these conditions the most important is epididymitis, and the differential diagnosis occasionally presents some difficulty, especially in cases of epididymitis following trauma. In this connection I have reviewed the cases of so-called traumatic epididymitis which I have observed, to learn whether any of them might have been instances of torsion. In some cases the observer's notes were inadequate for a certain diagnosis at this late date, but it seems to me significant that in only one instance labeled traumatic epididymitis did atrophy of the testicle result, and that was a case of rather extensive trauma to the suprapubic region, scrotum and thigh, accompanied by marked swelling and the formation of hematoma.

In epididymitis the pain is not so sudden or so severe as in torsion; there is usually evidence of infection in the urine, prostate or seminal vesicles or a history of recent urethritis; the temperature is more apt to be elevated, and the epididymis is apt to lie in its normal relationship to the testicle and is likely to be firmer and larger than in torsion. Also in epididymitis the tenderness tends to be localized to the region of the epididymis, while in torsion the whole mass is equally tender. Again, in epididymitis there is likely to be tenderness and swelling of the vas, and elevation of the scrotum relieves rather than accentuates the discomfort. Moreover, at the age at which torsion is most common, epididymitis is uncommon.

Orchitis except as a complication of mumps and occasionally of influenza is rare; the pain is not usually severe, and the swelling, though extensive, does not involve the cord.

Torsion has occasionally been mistaken for strangulated hernia, and the differential diagnosis may be dif-

ficult, for an undescended testicle is more apt to be affected by torsion than a fully descended one and is commonly accompanied by a hernia. Of course the general symptoms of strangulated hernia are more severe than those of torsion, and they grow progressively more severe while those of torsion progressively ameliorate. Both conditions require prompt treatment, and at operation all doubt will be resolved.

Confusion with suppurative inguinal adenitis has been reported a few times. The absence of the testicle from the scrotum and the absence of any infection draining to the inguinal glands (chancroid, for example) should put one on the right track.

In one of our cases the diagnosis of acute hematocele was made first. The patient was seen late, three days after onset, at which time there were marked swelling and discoloration. A few similar instances are on record. With hematocele the pain is never so severe and there is not the retraction of the testicular mass seen with torsion.

Prompt diagnosis is important, for on it may depend the health of the affected testis. Of course if the twist has been sufficient to cause infarction, delay makes no difference; but if the patient is seen before necrosis has occurred, prompt diagnosis and prompt treatment may preserve the life of the affected testis.

The best treatment is immediate operation. The scrotum should be incised and the testicle delivered. If it is necrotic, it can then be removed; if it is not necrotic and if the twist is in the cord, the torsion can be relieved, and if it is intravaginal, the tunica can be slit and the twist reversed. In any event it is best to incise and invert the tunica and then suture the cord and testicle to the scrotal septum in such a way that torsion becomes impossible.

Sometimes spontaneous detorsion occurs, and sometimes manual detorsion is possible without incision; but in either event operation shortly thereafter is desirable to eliminate any possibility of recurrence.

In the majority of recorded cases, necrosis had occurred and either orchidectomy was done or atrophy followed.

In view of the fact that in twenty-four of 350 cases on record the condition was bilateral, and in view of the fact that congenital abnormalities such as might predispose to torsion tend to be bilateral, I advocate operation on the remaining testicle to prevent a like misfortune involving it.

REPORT OF CASES

CASE 1.—A youth aged 19, half an hour after doing some high diving, noticed an aching sensation in the scrotum. This was followed by marked swelling but not by discoloration. Examination three days later showed marked enlargement of the scrotal contents on the left side with extreme tenderness which made accurate examination impossible. The temperature was 99 F., and there were no general symptoms. The swelling gradually receded, and the patient returned to school. Two years later physical examination showed the left testis atrophic, firm and insensitive.

It is possible that, had this condition been recognized immediately, prompt operation would have saved the testis.

CASE 2.—A youth aged 17 for six years had recurrent attacks of pain and swelling of the left testicle. The symptoms came on suddenly, disappeared rather quickly and were not associated with fever. At the end of the last attack, as it was subsiding, the testicle swelled again and there was a temperature of 101 F. When I saw the testicle three months later it was still larger than the right and was firm, somewhat irregular in shape and insensitive. The Wassermann test and the Aschheim-Zondek test were negative. It is my impression that the patient had recurrent attacks of incomplete torsion, eventuating in an attack of complete torsion with gangrene and probably infection.

There was every opportunity of saving this testicle by operation, either during an attack or between attacks. I have advised a prophylactic operation on the other testicle.

CASE 3.—A boy aged 13 awoke one morning with pain in the left testis without any apparent cause. A few hours later, when he was examined, there were moderate swelling and exquisite tenderness of the left testis. The seminal vesicles were not palpable, and there were no urinary symptoms. A diagnosis of torsion was made and an attempt made to untwist the testis. This was unsuccessful and apparently increased the pain. Operation was therefore performed, about twelve hours after the onset of symptoms. At operation the testis was found to be mottled but not black. There were two twists of the testis on the cord, and these were released; the testis was replaced and sutured in such a way that torsion would be impossible in the future. This testis is now shrunken to half the size of the other and is firm and insensitive. Since then I have operated on the other testis and have sutured it in such a manner that a twist would be impossible.

It might have been wiser in this case not to have attempted manipulative detorsion and to have operated immediately, though the probabilities are that the torsion was complete from the first.

CASE 4.—A man aged 22 while doing some heavy work noticed pain in the right inguinal region, and later swelling appeared. There were no fever, no history of venereal disease, no abnormality of the prostate or seminal vesicles and no urinary symptoms. The right testicle was markedly swollen and tender. At operation the epididymis was found to be anterior to the testicle; both testis and epididymis were dusky, especially the epididymis, and neither bled when punctured The testis was removed and found to be completely infarcted.

I would now advise operation on the other testicle.

CASE 5.—A boy aged 7 years for several weeks complained repeatedly of discomfort in the right side of the scrotum, which was relieved on some occasions by lifting and rotating the testicle. In one attack the testicle became somewhat swollen, and operation was decided on. At operation the right testicular mass was found to be twice normal size. The tunica was thick and edematous, and the testis lay within it, upside down. The tunica was inverted about the cord, and the cord and testis were sutured to the septum. The boy has been completely relieved of symptoms and the testis seems normal.

CASE 6.—A strong, well developed boy of 13 noticed an ache in his lower left quadrant after a boy scout hike, and his left testicle became swollen, tense and tender. His physician advised a suspensory. Two weeks later, when seen by me, the left testicular mass was three times normal size, tense, firm and not at all tender and did not transmit light. A month later it was about normal in size but was unduly firm. The patient has not been heard from for eight years, but the testis is probably atrophic.

I would now advise operation on the other testis.

CASE 7.—A man aged 38 without any apparent reason had pain in the right groin which later involved the right testis. When he was first seen, a week later, his temperature was normal, his urine was clear, there was no urethral discharge and the prostate gave no evidence of infection. The right testicle was held high in the scrotum, and the epididymis was somewhat swollen, firm and tender and lay somewhat lateral to the testis. Ten days later the epididymis was still enlarged and a little indurated.

In the absence of any evidence of infection, I considered this a case of incomplete torsion.

CASE 8.—A man aged 34 noticed one night that without cause his left testis had swelled and become tender. The next day the swelling became less and the tenderness largely disappeared. The epididymis was found to be somewhat swollen and lay lateral to the testis. Four days later there was no abnormality.

This was undoubtedly a case of partial torsion, with spontaneous detorsion. The patient has not been seen for six years. Under similar circumstances I would now advise operation to prevent recurrence.

CASE 9.—A young man aged 19 was seized with sudden terrific pain in the left lower quadrant of his abdomen, with no apparent cause, and became nauseated and vomited. There were no urinary symptoms. He was rushed to the hospital by his friends. Examination showed slight tenderness in the left lower quadrant. The left testis was drawn up high in the scrotum and was extremely tender. The cord and testis were manipulated, with spectacular and immediate relief of symptoms. He has not returned for observation but two years later is reported to be in good health and to have had no more attacks. I have advised him to have the testis operated on to prevent recurrence.

CASE 10.—A boy aged 4 years was brought in by another physician with a diagnosis of strangulated testicle. Operation showed torsion and infarction. The testicle was removed.

In such a case I would now advise operation on the other side.

CASE 11.—A physician aged 27 complained of a sudden attack of epididymitis and gave a history of repeated sudden attacks of pain and swelling of the left testis, with recovery in a day or two. The attacks usually followed slight trauma, though in a few instances there was no exertion or trauma to explain it. There had been at least twenty-five attacks during the past twelve years, and the patient had consulted many physicians, surgeons and urologists, who had all made a diagnosis of epididymitis. He was seen by us in three attacks and was taught to undo the twist immediately after it occurred. There was always one complete twist clockwise. He has been so successful in detorsion that, although there have been several attacks since, he has never come in for the operation which was recommended.

CASE 12.—A man aged 42 complained of pain in the right side of the abdomen, which had come on suddenly two days before, during coitus. The pain had been intermittent, had not radiated and had not been accompanied by urinary symptoms or by nausea or vomiting. There was no history of previous attacks. There was some tenderness and muscular resistance on the right side of the abdomen, with its maximum in the region of McBurney's point. The right testis was absent from the scrotum. A McBurney incision was made and a mass found consisting of a black and swollen testis, with one complete twist to the pedicle. It was removed with the appendix, which showed signs of mild chronic appendicitis.

SUMMARY AND CONCLUSIONS

I have reviewed briefly the symptoms and results in cases of torsion of the testicle and have reported twelve new cases. I wish to emphasize the importance of prompt recognition of this condition and would stress the following elements in the diagnosis: 1. The age of the patient. In this series eight patients were under 23, the youngest being 4 years old and five being adolescents. 2. The sudden onset. 3. The severity of the pain. 4. The absence of history or evidence of genitourinary infection. 5. The position of the affected testicle in the scrotum. 6. The position of the epididymis with reference to the testicle. 7. The tenderness of the testicle. 8. Prehn's sign.

Finally, I would emphasize my conclusions regarding treatment. I believe that in an acute attack prompt operation offers the best chance of a healthy testicle; that even though an attack is relieved by manual or spontaneous detorsion, operation should be done soon to prevent recurrence, and that if, because of torsion, a testis has become atrophic or has been removed, operation should be done on the remaining testis to prevent a like fate befalling it.

ABSTRACT OF DISCUSSION

DR. ROGER W. BARNES, Los Angeles: Torsion of the testicle is probably undiagnosed more often than it is recognized. Not long ago a patient was referred to me, and both the referring pediatrician and the hospital house officer stated that he had never before heard of the condition. Dr. Ormond's report of twelve cases shows that he has been on the alert to recognize the condition. I should like briefly to report a case in which there were unusual symptoms. A boy aged 14 was awakened by a sudden severe pain in the left testicle. A physician was called, who found the testicle extremely tender and slightly swollen and the cremasteric muscle contracting and relaxing so that the movement of the scrotum was very noticeable. The next morning the pain in the testicle was still present but not severe. The patient, however, complained of frequent urination and urgency and of having noticed some blood at the end of urination. The temperature was 103 F., and further examination showed the testicle to be very tender but no larger than it had been the night before. There was considerable tenderness in the lower left part of the abdomen just above the groin. When I saw the patient that afternoon the temperature was 101.2 F., and the other manifestations were approximately the same as those observed in the morning. The testicle was tipped somewhat upward, so that the isthmus of the epididymis was below instead of posterior to the testicle. Urinalysis showed many red blood cells, an occasional pus cell and a few gram-negative rods and gram-positive cocci. A roentgenogram showed no evidence of urinary calculi. The leukocyte count was 9,200. At operation some edema of the cord was found, but no torsion was present. The testicle was somewhat congested but otherwise normal. Fixation of both testicles, as Dr. Ormond has advised, was done, and the boy made an uneventful recovery. I am not certain whether some other pathologic process produced the fever, the tenderness in the lower left part of the abdomen and the blood in the urine, or whether these manifestations were all due to the torsion of the testicle. I should like to have Dr. Ormond's opinion regarding this.

DR. JAMES A. MAY, San Diego: Dr. Ormond has given a comprehensive discussion of torsion of the testicle. The twelve cases which he has reported constitute a rather large individual series and give his paper especial value and interest. There has been considerable speculation regarding the underlying etiologic factors in torsion. A thorough knowledge of the embryologic development of the testis and the mechanism of testicular descent is necessary for a complete understanding of the abnormal anatomic characteristics. The predisposing factors, according to Hinman, are (1) an anomaly of the tunica vaginalis which may be too large or have too high an insertion on the cord or an abnormal reflection from the epididymis; (2) absence or too great length of the gubernaculum; (3) an unusually low insertion of the cord; (4) an anomaly of the attachment of the epididymis to the testicle making the mesorchium loose or too short, and (5) an anomaly of the attachment of the testis and epididymis to the scrotum, so that this attachment is too loose. A voluminous tunica vaginalis per se would not seem to be a logical etiologic factor if one may judge from the frequency with which hydrocele occurs. I believe that the abnormal reflection from the epididymis is a much more important factor, in that it allows the testicle and the epididymis to hang in an intravaginal position which invites torsion. Absence or too great length of the gubernaculum does not seem to constitute a logical offender, since intermittent testicular retention is common in boys. The abnormal or loose attachment of the epididymis to the testicle, which causes the testicle to hang in an eccentric manner, is a much

more important factor. In addition, there are external factors which concern the force that precipitates the twist. Violent trauma, such as a direct blow, may tear the testicle loose from its scrotal attachments, thus permitting torsion to occur. Torsion has followed walking, heavy lifting, sneezing or straining at stool. It has also occurred during sleep. Many writers believe that a strong contraction of the cremasteric muscle initiates the twist, but this cannot be considered a factor in the causation of abdominally retained testes. The conclusion regarding the cause of torsion is that no one factor is responsible in all cases and that several factors may play a part in any one case.

DR. JOHN K. ORMOND, Detroit: I have never seen a case like the one described by Dr. Barnes. Hematuria has not occurred in any of the cases I have observed. Dr. Barnes's emphasis on teaching is apropos. I thank Dr. May for his discussion of the cause, which adequately complements my paper.

EXCRETION OF SULFANILAMIDE AND ACETYLSULFANILAMIDE IN HUMAN MILK

SHERMAN S. PINTO, M.D.
OMAHA

With the introduction and widespread use of sulfanilamide in the treatment of puerperal infections, much work has been done on the effect of the drug on the sick mother.[1] The excretion of the drug in men and in nonlactating women has also been studied extensively,[2] but I have been unable to find any work on the excretion of sulfanilamide in the lactating human mother. This work was undertaken to study the possibility of excretion of sulfanilamide in human milk and to determine, if possible, the amount of both sulfanilamide and the conjugated form of sulfanilamide which are known to be present in human blood [3] and, therefore, could possibly be present in human milk.

PROCEDURE

The method described by Marshall [2] in which alcohol is used as a protein precipitant cannot be applied to milk because of the high fat content of milk. An appreciable amount of fat is dissolved by the concentrated alcohol and later is precipitated during the process of diazotization. In cow's milk, the method described by Fuller,[4] in which trichloroacetic acid is used as a protein precipitant, works satisfactorily. Apparently there is enough protein present so that the fat of the milk is enmeshed by the protein coagulum, and fat and protein are removed at the same time. In human milk the ratio of fat to protein is much higher, and the protein precipitants that I used failed to form a coagulum which would at the same time enmesh and remove all the colloidal fat. I have overcome this difficulty by making the analyses on "skimmed" human milk. The milk is centrifuged for ten minutes at 3,500 revolutions per minute. Sulfanilamide added to human milk has been recovered quantitatively from the skimmed portion of the milk, and none was lost by dissolving in the fat which was removed by centrifugation. Since the fat content of the milk in the "cream" layer varied from 3 to 4.5 per cent, it was found more satisfactory to report all results in terms of "skimmed" milk. Diazotization of the sulfanilamide with dimethyl-alpha-naphthylamine was used because the color produced was extremely sensitive to small variations of the sulfanilamide content of the sample undergoing examination. Certain conditions were found to produce maximum color, deviations from this optimum resulting in lessened color production. The conditions for optimal results are that (1) the solution should contain 0.01 normal hydrochloric acid, (2) the solution should contain 47 per cent alcohol and (3) the trichloroacetic acid concentration should be kept as low as possible because it retards the diazotization process. To 1 cc. of skimmed milk are added 1 cc. of 20 per cent trichloroacetic acid and 2 cc. of water. The mixture is filtered, and 2 cc. of the clear filtrate is pipetted into a 15 cc. test tube. To this are added in succession 1 cc. of tenth normal hydrochloric acid, 5 cc. of 95 per cent alcohol, 1 cc. of 0.1 per cent sodium nitrite and, after waiting three minutes, 1 cc. of the dimethyl-alpha-naphthylamine reagent. (The dimethyl-alpha-naphthylamine reagent is made by dissolving 1 cc. of dimethyl-alpha-naphthylamine in 95 per cent ethyl alcohol and diluting to 100 cc.) A suitable standard should be prepared at the same time. It is important that the standard should also contain trichloroacetic acid, for this imparts an orange tinge to the final color, thus facilitating the color comparison. Maximum color development occurs in thirty minutes and remains constant for several hours.

It has been shown that, at least for dogs, acetylsulfanilamide is more toxic than free sulfanilamide. Therefore, I have extended my studies to include determination of this substance in human milk. When a protein-free filtrate of milk, prepared by using trichloroacetic acid, is heated with normal hydrochloric acid to hydrolyze the acetylsulfanilamide compound, the solution turns brown after about ten minutes heating at boiling temperature. I found that this charring is due to some substance or substances which are removable by treatment of the filtrate with copper sulfate-calcium hydroxide, as is done for the removal of carbohydrates. To use copper sulfate-calcium hydroxide for the removal of protein and carbohydrate, as is done for the determination of lactic acid in milk, is not suitable, since some substance is left in solution which is precipitated by the alcohol at the time of diazotization of the sulfanilamide. I found that the copper sulfate-calcium hydroxide treatment did not remove any sulfanilamide added to human milk.

Ten cc. of protein-free filtrate, prepared by adding one volume of 20 per cent trichloroacetic acid to one volume of milk and filtering, is pipetted into a 25 cc. volumetric flask. To this is added 4 cc. of 20 per cent copper sulfate and 4 cc. of a 20 per cent calcium hydroxide suspension. If the calcium hydroxide suspension has not been freshly prepared, more than 4 cc. may be necessary in order to make the contents of the flask alkaline. The contents are shaken frequently for one-half hour, diluted to 25 cc. and filtered. Five cc. of the filtrate (equivalent to 1 cc. of milk) plus 1 cc. of six normal hydrochloric acid are put into a test tube 25 by 200 mm., covered with a small beaker and placed in boiling water for thirty minutes. After

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Eli Lilly & Co. furnished the sulfanilamide used in this work.

From the University of Nebraska College of Medicine, Department of Biochemistry.

Dr. Sergius Morgulis showed continued interest and gave advice throughout the course of this work.

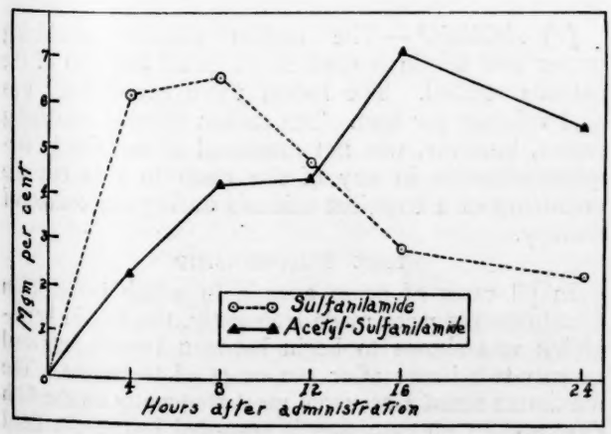
1. Colebrook, Leonard, and Kenny, Méave: Treatment of Human Puerperal Infections and Experimental Infections in Mice with Prontosil, Lancet **1**: 1279 (June 6) 1936.
2. Marshall, E. K., Jr.; Emerson, Kendall, and Cutting, W. C.: Para-Aminobenzenesulfonamide, J. A. M. A. **108**: 953 (March 20) 1937.
3. Marshall, E. K., Jr.: Determination of Sulfanilamide in Blood and Urine, J. Biol. Chem. **122**: 263 (Dec.) 1937.
4. Fuller, A. T.: Para-Aminobenzenesulfonamide in Prontosil Therapy, Lancet **1**: 194 (Jan. 23) 1937.

cooling, one drop of phenolphthalein is added and the hydrolized mixture is neutralized with concentrated sodium hydroxide solution. The liquid is then transferred to a 10 cc. volumetric flask and diluted to volume. Five cc. of this diluted material (equivalent to 0.5 cc. of milk) is pipetted into a 25 cc. test tube and the analysis for sulfanilamide is made as originally described by Marshall [2] for sulfanilamide in urine. To the 5 cc. of filtrate are added 5 cc. of water, 2 cc. of tenth normal hydrochloric acid, 5 cc. of 95 per cent ethyl alcohol, 1 cc. of 0.1 per cent sodium nitrite and 1 cc. of the dimethyl-alpha-naphthylamine reagent. It is not necessary to treat the standard with trichloroacetic acid, copper sulfate or calcium hydroxide. The trichloroacetic acid in the milk filtrate is decomposed on hydrolysis and does not affect the final color produced. The copper sulfate-calcium hydroxide treatment of the filtrate does not influence the color production.

CLINICAL RESULTS

In the lactating woman a study was made of the excretion of both sulfanilamide and the acetylated compound in the milk and urine.

The patients used in this report had been delivered of normal babies several days previously and had normal kidney function. During the period of the study the babies were placed on an artificial formula. The patients were given 4 Gm. of sulfanilamide in divided doses at 7, 8 and 9 a. m. For the next twenty-four hours no change was made in the diet or fluid intake. The urine was collected for twenty-four hours and the total amount of sulfanilamide and acetylsulfanilamide excreted in it was determined.[2] The milk was collected every four hours, the breasts being pumped dry, and determinations of the sulfanilamide and acetylsulfanilamide content were made for the twenty-four hour period. The entire amount of sulfanilamide administered was not excreted during that time but the amount left in the body was not sufficient to influence the results. Table shows the results obtained.



Excretion of sulfanilamide and acetylsulfanilamide in human milk.

On the chart and in the table it can be seen that the peak of excretion of conjugated sulfanilamide in milk occurs several hours later than the peak of excretion of free sulfanilamide in milk. Both these curves are similar in shape to the concentration of sulfanilamide in the blood as described by Marshall,[2] with the difference that in blood the peak of the concentration of the drug occurs several hours earlier than it does in the milk.

COMMENT

The concentration of sulfanilamide in human milk after the ingestion of a single large dose of the drug follows a course similar to that found by other workers for its concentration in blood.[5] The only difference is that the peak of concentration in milk seems to lag behind that in the blood by several hours. The concentration of acetylsulfanilamide in milk has a similar concentration curve except that the peak of concentration occurs several hours later than the peak for free sulfanilamide. Analysis of separate samples of milk shows no tendency on the part of the breast tissue to concentrate the drug in the milk. In fact, from the evidence at hand it would seem that the concentration of the drug in the milk is directly dependent on the level in the blood and that when the blood level falls there is a similar fall in the level of sulfanilamide in the milk. This would seem to be accomplished by reabsorption of the drug into the blood from the milk, thus tending to prevent dangerous accumulation of the drug in the milk. This mechanism prevents nursing infants from ingesting harmful amounts of the drug from the milk.

Excretion of Sulfanilamide and Acetylsulfanilamide in Human Milk for the First Twenty-Four Hours After Ingestion by Mouth

		Milk					Urine		
			Sulfanilamide Content		Acetylsulfanilamide Content				
Patient	Hours After Drug Administration	Volume, Cc.	Mg.	Mg. %	Mg.	Mg. %	Volume, Cc.	Sulfanilamide, Gm.	Acetylsulfanilamide, Gm.
L. K.	4	31	1.9	6.1	0.7	2.2			
	8	75	5.0	6.6	3.2	4.3			
	12	90	4.2	4.7	4.0	4.4			
	16	112	3.3	2.9	8.5	7.6			
	24	120	2.8	2.3	6.6	5.5			
	Total	428	17.2		23.0		3,225	2.60	0.33
M. T.	4	39	1.2	3.0	2.3	5.9			
	8	32	2.0	6.1	2.0	5.2			
	12	21	0.9	4.3	1.4	6.6			
	16	36	1.2	3.2	2.9	8.1			
	24	43	1.1	2.5	2.6	6.0			
	Total	171	6.4		11.2		1,500	1.49	0.23
D. M.	4	18	0.9	5.0	0.3	1.5			
	8	70	4.1	5.9	1.3	1.9			
	12	43	1.6	3.7	1.9	4.4			
	16	22	0.6	2.9	1.0	4.5			
	24	132	2.3	1.7	5.3	4.0			
	Total	285	9.5		9.8		3,400	2.44	1.54

A study of the figures for L. K. in the table shows that, while the patient secreted 428 cc. of milk during the twenty-four hour test period, this milk contained a total of only 17.2 mg. of free sulfanilamide and 23 mg. of acetylsulfanilamide, calculated as sulfanilamide. More than half the dose of sulfanilamide was excreted through the kidneys in the first twenty-four hours after administration. This is certainly an example of the general principle that noxious drugs are rarely secreted in the milk of nursing mothers in quantities sufficiently large to harm the nursing infant.

Theoretically, any nursing baby under 1 year of age will not take more than 1,200 cc. of milk a day. If the mother's blood level of sulfanilamide should be kept at 10 mg. per hundred cubic centimeters for the full twenty-four hours, the baby would not receive more than 0.12 Gm. of sulfanilamide and about 0.16 Gm. of acetylsulfanilamide. This dosage of the drug would not be harmful to any baby except one very allergic to sulfanilamide.

5. Scudi, J. V.: Determination of Sulfanilamide in Biological Media, J. Biol. Chem. **122**: 539 (Jan.) 1938. Marshall, Emerson and Cutting.[2]

SUMMARY

A method has been devised for the determination of sulfanilamide and acetylsulfanilamide.

From the limited series reported, it would seem that the amounts of sulfanilamide or acetylsulfanilamide excreted in human milk, when therapeutic doses are given to the lactating mother, is not ordinarily harmful to the normal nursing infant.

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ANEMIA DURING SULFANILAMIDE THERAPY

W. BARRY WOOD JR., M.D.

BALTIMORE

Acute anemia associated with the administration of sulfanilamide was first described by Harvey and Janeway.[1] Three cases were reported, and the accounts of two additional cases were later published by Kohn [2] and Willis.[3] Except for these few reports very little emphasis has been laid on the development of severe anemia as a complication of sulfanilamide therapy.

During the past year 522 patients have received sulfanilamide [4] in the Johns Hopkins Hospital. By far the commonest serious toxic complication observed in this series of cases has been the development of acute anemia. A special study of the cases in which anemia developed has been undertaken and the significant data obtained are reported in this paper.

INCIDENCE

The incidence of acute anemia associated with sulfanilamide therapy is considerably higher than one might judge from the scarcity of reports in the literature. Among the 522 patients treated with sulfanilamide acute anemia developed in twenty-one, or 4 per cent. It is of interest that the incidence among children was higher than among adults. One hundred and forty-four children received the drug and acute anemia developed in twelve (8.3 per cent), whereas there were only nine cases of acute anemia among the 378 adults treated (2.4 per cent). Agranulocytosis was much less common than acute anemia, there having been but one case in the entire series.

PREDISPOSING FACTORS

No definite predisposing factors were noted in the analysis of cases of acute anemia, but the following should be discussed briefly:

(*a*) *Type of Infection.*—The twenty-one patients in whom acute anemia developed were suffering from various types of both acute and chronic infections, as listed in table 1. No one form of infection seemed to predominate.

(*b*) *Fever.*—It may possibly be of significance that all twenty-one patients had fever (in most cases over 102 F.) at some time during the period of sulfanilamide therapy. No cases of acute anemia occurred among a large group of afebrile patients who were given sulfanilamide for prophylactic reasons or because of chronic bacilluria. In one patient, a 2 months old infant, during a high fever severe anemia developed after three days of treatment, but later, when she was afebrile, anemia failed to develop when a second course of the drug was given. Whether or not the presence of fever predisposed to the development of anemia in these cases remains open to question.

(*c*) *Dosage.*—The patients in whom acute anemia developed did not receive on the average any larger doses of the drug than the other patients treated with sulfanilamide. The largest dose given was 0.2 Gm. per kilogram of body weight in twenty-four hours, whereas as much as 0.47 Gm. per kilogram has been given in other cases with apparently no harmful effects.

(*d*) *Concentration of Sulfanilamide in the Blood.*—The highest concentration of sulfanilamide encountered in the blood was 10.7 mg. per hundred cubic centimeters. Blood levels as high as 40 mg. have been observed among patients in whom anemia has not developed.

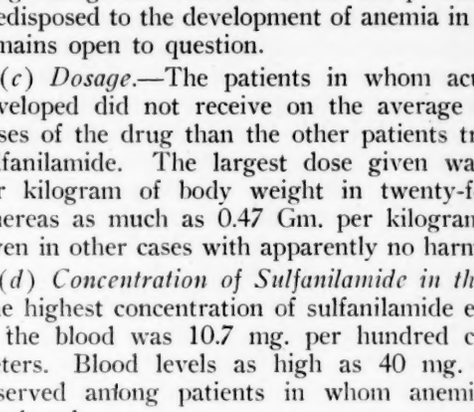

Chart 1.—Date of maximum anemia in cases of acute anemia associated with sulfanilamide therapy. Two cases were not charted because of insufficient data. Both hospital admissions of T. L. are included.

(*e*) *Acidosis.*[5]—The carbon dioxide combining power was within normal limits in all but two of the patients studied. The lowest value encountered was 33.4 volumes per cent. The carbon dioxide combining power, however, was not measured at sufficiently frequent intervals in any of the cases to rule out the possibility of a transient acidosis during the course of therapy.

TIME RELATIONSHIP

In all cases of acute anemia in which hemoglobin measurements were made frequently, the fall in hemoglobin was shown to begin between twenty-four and seventy-two hours after the onset of treatment. The maximum anemia occurred most frequently on the fifth day, and in no case was it recorded before the third day or after the seventh day (chart 1). It should be emphasized that in the entire series of 522 cases in which sulfanilamide therapy was used no rapidly progressing anemias developed after the first week of therapy except when there was an obvious cause such as loss of blood at operation.

A second type of anemia observed occasionally during sulfanilamide therapy has been reported by Jennings and Southwell-Sander [5] and might be termed a "slow

From the Medical Clinic of the Johns Hopkins Hospital and University.

1. Harvey, A. M., and Janeway, C. A.: The Development of Acute Hemolytic Anemia During the Administration of Sulfanilamide, J. A. M. A. **109:** 12 (July 3) 1937.

2. Kohn, S. E.: Anemia During Treatment with Sulfanilamide, J. A. M. A. **109:** 1005 (Sept. 25) 1937.

3. Willis, Thayer: Sulfanilamide in Ophthalmia Neonatorum, Yale J. Biol. & Med. **10:** 275 (Jan.) 1938.

4. The great majority of the patients were treated with sulfanilamide; a few received the closely related compound prontosil (the disodium salt of 4-sulfamido-phenyl-2'-azo-7'-acetylamino-1'-hydroxynaphthalene-3', 6' disulfonic acid). The cases are reported through the courtesy of Drs. Perrin H. Long and Edwards A. Park.

5. Jennings, G. H., and Southwell-Sander, G.: Anemia and Agranulocytosis During Sulfanilamide Therapy, Lancet **2:** 898 (Oct. 16) 1937.

anemia." The fall in hemoglobin progressed slowly in their three cases, the maximum anemia occurring from two to four weeks after the start of treatment. My associates and I have observed eight similar cases of "slow anemia," but, since it is extremely difficult to determine in most instances whether the anemia is due to sulfanilamide or is secondary to a long standing infection, I have not included them in the present analysis.

NATURE OF ANEMIA

In their original publication, Harvey and Janeway described the acute anemia occurring during sulfanilamide treatment as a hemolytic anemia. Studies on the blood of their three patients indicated that there was rapid hemolysis associated with the fall in hemoglobin. Recently we have had the opportunity of following the entire course of a recurrent acute anemia which developed during a second course of sulfanilamide treatment. Because of the completeness of the data obtained, the case is reported in some detail:

REPORT OF CASE

T. L., a Negro chauffeur aged 36, first admitted to the Johns Hopkins Hospital March 15, 1937, complained of a severe sore throat. His general health had been excellent in the past. In 1922 he had had a peritonsillar abscess which required incision and drainage. Since childhood he had had frequent rather mild sore throats. Two days before admission to the hospital a cold in the head developed followed by a sore throat, which became progressively worse until he came to the hospital.

The clinical and laboratory examinations as well as the patient's course in the hospital during his first admission have been reported in detail by Harvey and Janeway (case 1) and need only be outlined briefly. The temperature was 104 F., pulse rate 110 and respiratory rate 40 per minute. The patient appeared acutely ill. No abnormalities were noted on physical examination except enlarged tonsils covered with flecks of yellowish exudate and tender lymph nodes palpable at the angles of the mandible. The blood was normal except for a leukocyte count of 19,000. Culture of material from the throat showed 95 per cent beta hemolytic streptococci.

Sulfanilamide therapy was begun on the first day and the patient received 21 Gm. of the drug over a period of five days. On the third day the throat infection appeared to be clearing and the temperature and white blood cell count had fallen to normal. The patient, however, complained of nausea and dizziness and, when two days later the temperature rose to 102.6 F., the drug was stopped promptly. On the seventh day it was noticed that the mucous membranes were pale and the scleras were jaundiced. Examination of the blood revealed a hemoglobin content of 30 per cent, a white blood cell count of 87,000 and changes in the blood smear indicative of increased activity of the bone marrow. The urine showed large amounts of urobilin but the serum bilirubin was not appreciably increased. The patient was given three transfusions during the next three days and recovery was rapid and uneventful. Just before discharge from the hospital he was given a test dose of 0.9 Gm. of sulfanilamide with no demonstrable effect on the blood.

March 6, 1938, nearly twelve months after his first admission, the patient was readmitted to the hospital with a severe sore throat of five days' duration. For two days he had had great difficulty in swallowing.

The temperature was 101.8 F., pulse rate 118 and respiratory rate 22. The patient appeared acutely ill and complained of great pain on swallowing. Again there were no abnormalities made out on physical examination except for tender enlarged cervical lymph nodes and inflamed tonsils covered with patches of white exudate. The tonsils were so swollen and edematous that they nearly met in the midline and threatened to close off the pharynx entirely. There was a slight swelling in the left peritonsillar region suggestive of an early peritonsillar abscess. Again there was a predominance of beta hemolytic streptococci in the throat culture.

As shown in chart 2,[6] examination of the blood revealed nothing remarkable except a white blood cell count of 18,900. The blood smear was normal. There was no immediate or twenty-four hour sickling and no increase in the fragility of the red blood cells. The icterus index was 7, examination of the urine was negative for urobilin and the van den Bergh test showed no increase in serum bilirubin.

TABLE 1.—*Cases of Acute Sulfanilamide Anemia*

Patient	Age Race Sex	Diagnosis	Days of Sulfanilamide Treatment	Total Dose of Sulfanilamide (Gm.)	Total Drop in Hemoglobin (per Cent)	Treatment of Anemia
T. L.	36 Negro ♂	Acute tonsillitis (2 admissions)	5 4	21.9 7.8	71 58	3 transfusions 1 transfusion
I. M.	26 Negro ♀	Peritonsillar abscess	2	6.7	52	2 transfusions
L. O.	53 White ♂	Carcinoma of bladder	3	7.2	60	5 transfusions
W. B.	62 White ♂	Gonococcic urethritis	5	24.0	31	3 transfusions
G. S.	27 Negro ♀	Gonococcic salpingitis	8*	31.2	45	2 transfusions
W. C.	19 Negro ♂	Lobar pneumonia	2	6.0	27	Iron therapy
B. L.	18 Negro ♀	Gonococcic arthritis	4	14.0	40	Iron therapy
H. C.	41 Negro ♂	Urinary tract infection	3	10.8	37	Iron therapy
V. R.	18 Negro ♂	Pneumococcic meningitis	3	13.2	50	3 transfusions
H. H.	8 Negro ♂	Acute tonsillitis	6	31.5	62	4 transfusions
M. J.	10 mos. White ♀	Meningococcic meningitis	6	11.0	25	2 transfusions
H. B.	10 Negro ♀	Generalized peritonitis	5	25.5	63	6 transfusions
J. M.	9 mos. Negro ♀	Urinary tract infection	3	5.8	40	3 transfusions
E. B.	7 mos. Negro ♂	Pneumonia	2	1.8	26	None
S. W.	7 mos. Negro ♀	Otitis media	3	4.5	42	None
R. G.	6 White ♂	Pharyneal abscess	4	14.4	35	2 transfusions
S. C.	2 Negro ♂	Pulmonary tuberculosis	5	7.0	31	None
M. M.	12 White ♀	Pyelonephritis	10†	18.0	28	2 transfusions
C. D.	10 mos. Negro ♀	Influenza bacillus septicemia	2	3.6	29	4 transfusions
R. A.	7 mos. Negro ♂	Staphylococcic septicemia	4	4.8	46	None
V. F.	4 Negro ♀	Scarlet fever	5	15.0	28	None

* Second hemoglobin determination not made until eighth day.
† Maximum anemia on fifth day. Patient was given two transfusions but the drug was not discontinued until five days later.

At the time of admission the question was at once raised as to the advisability of treating the patient with sulfanilamide, in view of his previous experience. At that time only one report of recurrent anemia during sulfanilamide therapy had appeared in the literature.[3] We had followed one patient, a 9 months old female infant, in whom anemia failed to develop

6. The laboratory studies were carried out by Dr. R. P. Howard and Mr. R. L. Sewell.

during a second course of sulfanilamide after the child had suffered a severe anemia with the first course. In addition, as already mentioned, the patient in question had been given a test dose of sulfanilamide at the end of his first hospital admission without any demonstrable effect on the blood. It was therefore quite uncertain whether on this occasion hemolytic anemia would develop if sulfanilamide were given. Because of the severity of the streptococcic infection of the tonsils it was finally decided to give sulfanilamide cautiously

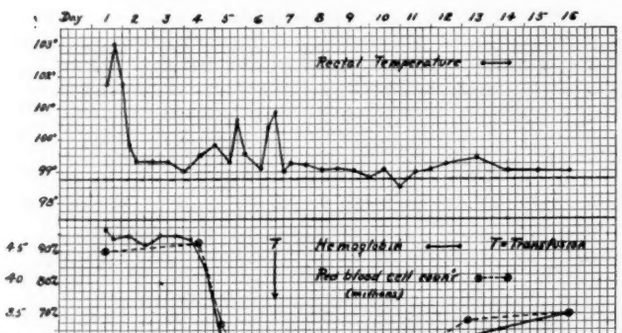
Day 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
Rectal Temperature
Hemoglobin
Red blood cell count (millions)
Reticulocyte count
White blood cell count
Icterus Index
Van den Bergh (mgm. %)
Urine Urobilin
Blood Sulfanilamide (mgm. %)
Sulfanilamide dose (Gms.)

Chart 2.—Results of blood and urine studies in case of acute hemolytic anemia associated with sulfanilamide therapy.

and watch the blood with great care in order that the drug might be stopped immediately if signs of anemia should develop.

Sulfanilamide was administered as shown in chart 2, a total of only 7.8 Gm. being given over a period of three days. The clinical response to the drug was dramatic. The temperature fell within twenty-four hours to 99.4 F. and the edema and inflammation in the throat subsided rapidly. The patient felt greatly improved on the third day, but in the afternoon he mentioned that he was slightly nauseated, and urobilin appeared in the urine. When the temperature rose to 100 F. on the following day and the hemoglobin, which was being checked every twelve hours, showed a slight drop, the sulfanilamide was stopped immediately. Fluids were forced to promote excretion of the drug through the kidneys and at the end of twenty-four hours the blood showed only a trace of sulfanilamide. In spite of the fact that the drug was stopped at the first signs of blood destruction, the anemia progressed rapidly during the next forty-eight hours, the hemoglobin finally falling to 40 per cent. The icterus index rose to 35, the van den Bergh reaction to 3.1 mg. per hundred cubic centimeters (indirect) and the patient became jaundiced and continued to excrete large quantities of urobilin in the urine. The reticulocyte count reached a maximum of 6.8 per cent on the fifth day. That the hemolytic process subsided as rapidly as it had begun is shown by the precipitous fall in serum bilirubin, which took place on the fifth and sixth days. The patient was given one transfusion of 500 cc. of citrated blood on the sixth day; thereafter he made an uneventful recovery.

Blood serum drawn on the fifth day showed large amounts of free hemoglobin identified spectroscopically. No free hemoglobin could be detected in the urine at any time. The urine from the fourth to the eighth day was a dark amber and Dr. E. K. Marshall was able to recover a reddish pigment by ether extraction which became colorless when reduced with zinc and showed absorption bands in the same range as certain of the porphyrins. The pigment has not as yet been clearly identified.

COMMENT

From the data obtained in this case as well as in the other cases already reported, it is quite evident that the development of acute anemia during sulfanilamide therapy is associated with rapid hemolysis. The abrupt rise in serum bilirubin as shown by the van den Bergh test and icterus index, the presence of excessive amounts of bile pigments in the urine and the demonstration of free hemoglobin in the blood plasma all point conclusively to an active hemolytic process. Kohn [2] has reported an additional sign of rapid hemolysis, namely hemoglobinuria. However, we have been unable to demonstrate free hemoglobin in the urine of any of the twenty-one patients in the present series except in one case which was complicated by gross bleeding from a carcinoma of the bladder.

EARLY DIAGNOSIS

The early signs of acute anemia associated with administration of sulfanilamide are well illustrated by the foregoing case and may be summarized as follows:

1. Nausea and dizziness usually begin from twelve to twenty-four hours before the signs of anemia are detected.
2. Increased excretion of urobilin in the urine is often the first laboratory evidence of increased destruction of the blood.
3. There is an unexplained rise in temperature on the third to the fifth day of therapy.
4. There is a sudden drop in hemoglobin.
5. Hyperbilirubinemia and jaundice are present.

TABLE 2.—*Cases of Acute Sulfanilamide Anemia in Which Second Course of Drug Was Given*

			First Course of Sulfanilamide Therapy			Second Course of Sulfanilamide Therapy			
Patient	Age Race Sex	Diagnosis	Days of Treatment	Total Dose (Gm.)	Drop in Hemoglobin (per Cent)	Days of Treatment	Total Dose (Gm.)	Drop in Hemoglobin (per Cent)	Interval Without Treatment
T. L.	36 Negro ♂	Acute tonsillitis	5	21.9	71	4	7.8	58	1 year
A. D.*	4 days Negro ♂	Ophthalmia neonatorum	14†	7.4	56	5	3.7	17	10 days
S. C.	2 Negro ♂	Pulmonary tuberculosis	7	14.0	20	5	7.0	31	5 months
S. W.	7 mos. Negro ♀	Otitis media	3	4.5	42	6	9.0	11	9 days
J. M.	9 mos. Negro ♀	Urinary tract infection	3	5.8	40	3	3.0	0	7 weeks

* Reported by Willis.[3]
† Second hemoglobin determination not made until eleventh day of treatment.

If every patient treated with sulfanilamide is carefully watched for the appearance of these signs, the diagnosis of acute hemolytic anemia can be made relatively early. It should be pointed out that even the earliest diagnosis may not prevent the development of a profound anemia. This is well illustrated by the case reported here, in which the anemia continued to progress rapidly in spite of the fact that the drug was stopped before the hemoglobin had dropped 10 per cent. Although the rapid fall in hemoglobin often cannot be

prevented by early diagnosis, it is only reasonable to suppose that the severity of the anemia can to some extent be controlled by early withdrawal of the drug.

RECURRENT ACUTE HEMOLYTIC ANEMIA

To date we know of five patients who have been given a second course of sulfanilamide in spite of the occurrence of acute anemia when they were first treated. In four of the five hemolytic anemia developed during the second course of therapy. The fifth patient escaped when treated a second time, but the absence of fever in this instance and the slightly smaller dose administered may have accounted for this exception. The data from these five cases are summarized in table 2 and serve to emphasize the danger of giving sulfanilamide to patients in whom acute hemolytic anemia has previously developed while under treatment with the drug.

PATHOGENESIS

Little is known about the pathogenesis of acute hemolytic anemia associated with sulfanilamide therapy. It is clear from studying the blood of patients suffering from this type of anemia that the drug acts either directly or indirectly on the red blood cells, causing hemolysis. There is no evidence that the anemia is in any way related to depression of the bone marrow, for in all the cases studied there have been signs of increased rather than of decreased hemopoiesis. However, no direct examinations of the bone marrow have been made. Thus far it has been impossible to reproduce the hemolysis by adding sulfanilamide to the blood in vitro. No sickle cell traits or increased fragility of the red blood cells have been detected in any of the cases. The Donath-Landsteiner test has consistently given negative results.

Acute anemia associated with sulfanilamide therapy must be classed as a drug idiosyncrasy, especially in view of the fact that the majority of patients who have once suffered an attack appear to be susceptible to recurrent attacks. The exact mechanism whereby the drug causes hemolysis must await further study of the blood of susceptible persons.

TREATMENT AND PROGNOSIS

The treatment of acute sulfanilamide anemia consists of two measures: (1) immediate withdrawal of the drug and (2) blood transfusion. That the first of these measures alone may not be effective, even when carried out early in the course of anemia, has already been emphasized. The response to blood transfusions has in all cases been satisfactory. No deaths from hemolytic anemia have been reported.

CONCLUSIONS

From the study of twenty-one cases of acute anemia associated with sulfanilamide therapy the following conclusions may be drawn relating to the management of patients under treatment:

1. The hemoglobin should be measured at daily intervals during the first week of treatment and once or twice a week thereafter as long as the treatment is continued. The urine should be examined frequently for urobilin during the first week, and all unexplained febrile reactions should be looked on with suspicion. The patient should be asked frequently about subjective symptoms such as nausea and dizziness, and jaundice should be carefully watched for.

2. At the first signs of the development of hemolytic anemia sulfanilamide should be withdrawn, fluids forced and the patient's blood matched for transfusion. If the hemoglobin falls to dangerously low levels, repeated transfusions are indicated.

3. Patients who have once suffered from acute hemolytic anemia during sulfanilamide treatment should not again be given the drug.

SUMMARY

1. Twenty-one cases of acute anemia associated with the administration of sulfanilamide, in a series of 522 patients treated with the drug, were studied. The incidence was higher in children (8.3 per cent) than in adults (2.4 per cent). No definite predisposing factors were noted in an analysis of the twenty-one cases.

2. The earliest signs of the anemia appeared between twenty-four and seventy-two hours after the onset of treatment. The maximum anemia occurred usually on the fifth day, and in no case did it occur before the third or after the seventh day.

3. The anemia has been shown conclusively to be associated with acute hemolysis, but the pathogenesis is at present not known.

4. Four out of five patients in whom acute anemia had developed when first treated with sulfanilamide suffered recurrences when a second course of the drug was given.

5. The anemia is treated by the immediate withdrawal of sulfanilamide, the forcing of fluids and blood transfusions. There have been no deaths reported.

6. It is important that the hemoglobin be watched carefully during the first week of sulfanilamide therapy.

Clinical Notes, Suggestions and New Instruments

RECOVERY FROM SUBACUTE INFECTIOUS ENDOCARDITIS FOLLOWING PRONTOSIL THERAPY

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Recovery from subacute infectious endocarditis is of such uncommon occurrence that the account of such a case seems worthy of record.

History.—O. H., a Negress aged 39, who entered the University of Kansas Hospitals April 13, 1938, complained of chills and sweats. The family history was negative. In 1930 the patient was admitted to this hospital with tonsillitis and arthritis. At that time a tonsillectomy was performed. She remained in the hospital from April 20 to May 4. Examination of the patient showed, in addition to the arthritis, a systolic murmur at the apex and a diastolic murmur over the aortic area and down the left sternal border. The diagnosis at that time was acute rheumatic fever, chronic tonsillitis, aortic insufficiency and mitral insufficiency.

The patient has been followed in the outpatient department for the past eight years and there are repeated notes regarding the presence of mitral and aortic murmurs. On several occasions she has shown marked cardiac failure. One month before admission to the hospital the patient had an abortion, which was followed by chilly sensations and some fever. This persisted only two days, following which she felt perfectly well. One week before the present admission the patient began feeling ill and complained of chills and sweats every afternoon; she had been "up and down in bed" most of the past week.

Examination.—At the time of admission the patient was lying listlessly in bed with a temperature of 100.8 F. Examination of the eyes showed several small petechial hemorrhages in the conjunctiva of the left eye and also a few petechiae on the left

From the Department of Internal Medicine, University of Kansas School of Medicine.

cheek and on the left side of the neck. The fingertips were painful, and one splinter hemorrhage under the nail was seen on the right index finger. The heart was enlarged; there was a loud rough systolic murmur at the apex and a soft blowing diastolic murmur over the aortic area. The liver extended two fingerbreadths below the left costal margin. The spleen was palpable and definitely enlarged.

The laboratory examination showed red blood cells 3,940,000, white blood cells 17,300, hemoglobin 62 per cent. The urinalysis showed a specific gravity of 1.025, a trace of albumin and from 6 to 8 pus cells per high power field. A blood culture taken April 13 was positive for Streptococcus viridans. Blood cultures taken April 14 and 15 were likewise positive. The organism grew very readily and was typical in every respect. The sedimentation index of the blood April 13 was 30 with a vertical curve.

The patient on admission was started on prontosil[1] 10 cc. intramuscularly twice a day, and 10 grains (0.65 Gm.) of sulfanilamide four times a day. This therapy was continued until April 23, on which day the prontosil was given intravenously three times. The sulfanilamide by mouth was omitted because of the extreme nausea which had developed. The patient received transfusions of 500 cc. of citrated blood on April 19, 26 and 28. The patient received 10 cc. of prontosil three times a day from April 23 until April 25 and twice a day from April 26 until May 13, at which time treatment with prontosil was discontinued.

The patient's temperature, which had varied between normal and 103 F., did not go above normal on April 26 and from that time on remained normal. Blood cultures taken on April 23 and 27 and May 2, 7, 11, 17 and 20 were negative. The spleen was not palpable May 5. The blood count May 7 revealed red blood cells 4,160,000, white blood cells 7,200, hemoglobin 74 per cent. This was a marked change, particularly in the white blood cell count, which on April 22 was 23,000. The blood sedimentation curves were as follows: April 26: index 32, vertical curve; May 3: index 17, diagonal curve; May 14: index 7, horizontal curve.

Although the patient continued to be fever free, signs of cardiac failure became more and more evident. The patient's dyspnea increased, and marked edema and anasarca appeared. The patient died May 25, twenty-nine days after the temperature had become normal and twelve days after treatment with prontosil had been discontinued. Autopsy was performed two hours after death by Dr. Rae Richeson of the department of pathology.

Autopsy.—The anatomic diagnosis was chronic and subacute vegetative bacterial valvulitis of the mitral and aortic valves (healing bacterial endocarditis), acute and chronic myocarditis, hypertrophy and dilatation of the heart. The heart weighed 400 Gm. The mitral valve showed marked thickening and scarring, and at the apex of one of the valve cusps was a vegetation which appeared to be healing and was covered with a thin layer of scar tissue. The aortic valves were also thickened and wrinkled, and on their edges were several vegetations which appeared old and organizing. Both valves were incompetent. Microscopic sections of the mitral and aortic valves showed evidence of extensive healing. On the aortic valve deep beneath the healed surface were some clumps of gram-positive diplococci. Cultures taken from small excised portions of the mitral and aortic valves were sterile.

COMMENT

Recovery from subacute infectious endocarditis is admittedly very rare. Since the remarkable results reported in certain streptococcic infections with prontosil and sulfanilamide, it is obvious that this drug should be tried in the treatment of subacute endocarditis. Hussey[2] reports one probable case of endocarditis in which recovery occurred after the use of sulfanilamide. The diagnosis in this case would, however, seem to be open to doubt. In our case there is no question as to the diagnosis. The patient had a history of rheumatic fever and old mitral and aortic valve lesions, petechiae, splinter hemorrhages, tender fingers, fever, enlargement of the spleen and three blood cultures positive for Streptococcus viridans. Necropsy showed the evidence of a recent endocarditis in the stage of healing and repair.

The question open to doubt is whether the cure was produced by prontosil or whether it was a spontaneous recovery. A review of the literature to March 1, 1938, comprising 309 articles, discloses no claims of a case of endocarditis cured with sulfanilamide. In 1925 the senior author[3] reported a case of subacute infectious endocarditis due to Streptococcus viridans but showing no embolic phenomena in which recovery occurred following the administration of intravenous gentian violet. Subsequent failures to influence this disease by the administration of gentian violet have led us to the conclusion that this was a case of spontaneous recovery, such as those reported by Oille, Graham and Detweiler,[4] which also showed no embolic phenomena.

There are, however, certain features of this case which suggest that prontosil acted as a curative agent. The fall in temperature, the disappearance of positive blood cultures, the change in the sedimentation curve, the disappearance of the enlarged spleen and the cessation of embolic phenomena, all following so closely the intravenous administration of prontosil, are highly suggestive. It is noteworthy that no change in the temperature occurred until prontosil was administered intravenously; also that the endocarditis was probably only of one month's duration and possibly only of one week's duration when therapy was instituted.

1. Prontosil is the disodium salt of 4-sulfamido-phenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′, 6′ disulfonic acid.

2. Hussey, H. H.: Probable Bacterial Endocarditis Apparently Cured with Sulfanilamide, M. Ann., District of Columbia **6**: 275-276 (Sept.) 1937.

3. Major, R. H.: Recovery from Subacute Infective Endocarditis Following Gentian Violet Therapy, J. A. M. A. **84**: 278-279 (Jan. 24) 1925.

4. Oille, J. A.; Graham, Duncan, and Detweiler, H. K.: Streptococcus Bacteremia in Endocarditis, J. A. M. A. **65**: 1159-1163 (Oct. 2) 1915; A Further Report on a Series of Recovered Cases of Subacute Bacterial Endocarditis, Tr. A. Am. Physicians **39**: 227-230 (May 6) 1924.

THROMBOPENIC PURPURA DUE TO FOOD ALLERGY

L. O. DUTTON, M.D., EL PASO, TEXAS

In January 1937 Squire and Madison[1] reported three cases of thrombopenic purpura that were found to be due to sensitization to food. These cases all conformed to the usual hematologic criteria for the diagnosis of the condition. All of the patients were relieved of their symptoms following the removal of the foods found to be the causative agents, and the symptoms returned on readdition of these foods to the diet. In view of the fact that many cases have been reported which showed thrombopenic purpura due to sensitization to drugs, and in view of the relationship shown by Squire and Madison between sensitization to certain foods and the thrombocyte level in the blood, it is evident that this etiologic possibility should be considered when these cases are encountered.

It is my purpose in this short communication to record another case in which food allergy was the etiologic factor in thrombopenic purpura.

REPORT OF CASE

History.—A. L. D., a white woman aged 59, was referred by Dr. Gottlieb Werley for blood study with the clinical diagnosis of purpura, probably due to an allergy to citrus fruits. The patient presented numerous ecchymotic spots distributed over the entire body. There were also innumerable petechial hemorrhages distributed over the forearms, thighs and legs. Ecchymoses had begun to appear about six years previously as occasional areas appearing on the limbs. There were free periods when there were no lesions. The bruises had increased in frequency and number until they were almost constantly present. It required about ten days for an area to clear after the hemorrhage appeared.

Ten days previous to the first visit there appeared numerous petechial hemorrhages over the limbs. This had never occurred before. For several days the number of petechiae increased. The petechiae followed the ingestion of a large quantity of citrus fruits while the patient was visiting in a citrus fruit raising community. The patient stated that she was not particularly fond of citrus fruits although she partook of one or the other of them frequently in small quantities. There were

1. Squire, T. L., and Madison, F. W.: Thrombocytopenic Purpura Due to Food Allergy, J. Allergy **8**: 143 (Jan.) 1937.

no subjective complaints, and the usual daily routine was being carried out as usual. Five days after the appearance of the petechiae a severe epistaxis occurred, which subsided to a slow capillary bleeding from the nasal membrane.

The essential points in the past history were as follows:

Head: Nasal congestion for many years.

Cardiorespiratory system: Normal.

Gastrointestinal tract: A marked anorexia and a distressing sense of fulness after even very small meals.

Genito-urinary tract: A severe hemorrhage after an operation on the kidney twenty-seven years previously. The details of this operation were not known. One year before admission there had been an attack of pain and hemorrhage from one kidney attributed to a stone, although no stone was demonstrable by complete x-ray and cystoscopic examination.

The menses had begun at 18 years and the menopause occurred at 52. Otherwise the menses were normal.

Other past illnesses were typhoid thirty years before and severe hives in childhood. There had also occurred the usual diseases of childhood.

The family history was insignificant except that the mother and one sister had had severe headaches for many years.

Other items in the past history were negative.

Examination.—The physical examination was negative except for the cutaneous lesions described. The abdominal wall was rather obese and satisfactory palpation of the spleen could not be accomplished.

Examination of the blood showed total white blood cells 5,600, total red blood cells 3,900,000, hemoglobin 12.5 Gm. per hundred cubic centimeters, neutrophil polymorphonuclear leukocytes 63 per cent, immature neutrophils 3 per cent, lymphocytes 28 per cent, eosinophils 5 per cent and basophils 4 per cent. There was slight irregularity in the size and shape of the red blood cells. In the stained smears only an infrequent platelet was seen. Direct enumeration of the platelets showed 60,000. There was no retraction of the clot after several days' standing.

The urine contained a trace of albumin, many pus cells and a few red blood cells.

Cutaneous reactions to food were negative. Intracutaneous reactions were definitely positive to orange, lemon, shrimp, avocado, apple, milk, rye, cheese and cottonseed. A number of other borderline reactions were obtained.

Leukopenic indexes were as follows: milk negative, wheat negative, egg borderline and orange positive.

A diagnosis was made of thrombopenic purpura, probably due to allergy to citrus fruits.

Progress.—The course of the condition confirmed the diagnosis. A diet was prescribed in which the foods giving positive reactions were omitted. No new ecchymotic areas appeared, although previously there were several new ones each day. Ten days after the diet was started the skin was practically clear. On this day the leukopenic index was done for orange juice. As already noted, the result was positive. The next day there were two large ecchymotic areas on the forearm. Before this test was done the platelet count had risen to 240,000 and the clot retraction time was normal. On the day after the test the platelet count was 100,000. After another month there had appeared no new lesions. Small amounts of citrus fruits were then added to the diet. After three days several small ecchymotic areas appeared on the limbs. The fruits were again removed from the diet and after four months there has been no return of the symptoms.

It is interesting to note that the anorexia and the sense of fulness after meals have disappeared. The platelet count is now 385,000. The remainder of the blood count is normal. The patient feels in better general health than she has for several years past.

COMMENT

Two thoughts seem to be indicated by this and other similar cases. First, the obvious one, that at least an unknown percentage of persons suffering from this disease might be relieved by a much simpler procedure than radical splenectomy. Certainly the results with this case were much more striking than those obtained by the more tedious and disappointing general therapy employed in the past.

Second, it is amazing that a shock organ could be so narrowly limited that only the cells responsible for the platelet formation in the bone marrow could be affected by an allergen or, on the other hand, that an allergic reaction should result in an abnormal function of the spleen (destruction of red blood cells).

SUMMARY

A case of thrombopenic purpura has been successfully and easily controlled by the removal from the diet of foods to which the patient was allergic.

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Special Clinical Article

CANCER OF THE CERVIX UTERI: RECOGNITION OF EARLY MANIFESTATIONS

CLINICAL LECTURE AT SAN FRANCISCO SESSION

KARL H. MARTZLOFF, M.D.

PORTLAND, ORE.

It is one thing to recognize cancer early, i. e. when it is first seen, but it is quite another to recognize early cancer, i. e. cancer in its incipience. It is to the recognition of early cancer that I shall confine my remarks.

When one considers that genital carcinoma comprises about 2 per cent of cancers in the male while it forms about 27 per cent of cancers in the female, its comparative importance is at once manifest. In general it may be said that of all women suffering from cancer about one third are afflicted with uterine cancer. Of these about 80 per cent have cancer originating in the cervix uteri.

The foregoing remarks would represent only statistical repetitions did they not develop the startling revelation that one of the organs most commonly involved in cancer in women is situated suitably for direct visualization, palpation and instrumentation as is no other human organ which has an equally high incidence of cancer. The obvious conclusion follows that the unequivocal diagnosis of established cancer of the vaginal portion of the cervix uteri generally is a simple matter and should follow closely on the first examination.

Equally important is it that so many patients who possess a so-called suspicious-appearing cervix, whatever that may be, should not be terrified by the fear of cancer and subjected to a long series of office treatments for the time-tattered, hysterical and questionable excuse of cancer prophylaxis, when it is possible to establish practically beyond peradventure the presence or absence of anything suggestive of cancer.

EARLY VISIBLE CANCER

This brings up at once the problem of recognizing the early manifestations of cervical cancers. Fortunately the majority of such cancers occur on the portio in the region about the external os. The primary prerequisites for their recognition are threefold: adequate exposure of the cervix, adequate illumination and deliberate, thoughtful inspection. There is little doubt that, if all physicians would observe these elementary

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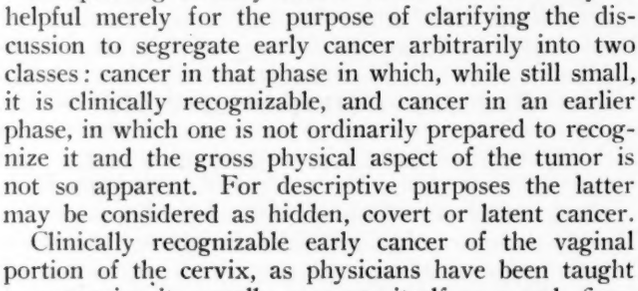
requirements, most cervical cancers would be suspected on the first examination, while they were still comparatively early yet advanced far enough to produce slight tumefaction, a small ulcer or some other superficial change outside the normal variation, although symptoms might be entirely lacking. One would then have the desirable combination of early recognition of comparatively early cancer.

In speaking of early cancer of the cervix it may be helpful merely for the purpose of clarifying the discussion to segregate early cancer arbitrarily into two classes: cancer in that phase in which, while still small, it is clinically recognizable, and cancer in an earlier phase, in which one is not ordinarily prepared to recognize it and the gross physical aspect of the tumor is not so apparent. For descriptive purposes the latter may be considered as hidden, covert or latent cancer.

Clinically recognizable early cancer of the vaginal portion of the cervix, as physicians have been taught to recognize it, usually presents itself as a red, firm, irregular, somewhat elevated circumscribed process, situated ordinarily in the neighborhood of the external os. It generally bleeds readily on light manipulation



Schematic representation of the method of obtaining material for histologic study. *A* represents a suspicious area on the anterior lip of the cervix uteri, with the dark lines indicating the direction of incisions for removal; *A'*, the shape of the excised block of tissue, and *B*, a larger suspicious area, which in some cases may advantageously be removed by a cone-shaped enucleation of the endocervix, together with a portion of the portio, as indicated by the circularly dotted line.

with a soft cotton pledget and on palpation may feel indurated, although induration as a highly diagnostic sign has probably been greatly overemphasized. It is a lesion that should at once arouse one's suspicion as to its malignant character, and to discover it no apparatus is necessary that cannot be found in the office of any qualified physician. The obtaining of tissue for histologic examination without undue delay is imperative, so that one's diagnosis may be unequivocally established and treatment advised.

The obtaining of biopsy material from such a suspicious area on the vaginal portion of the cervix is in itself so important a matter that it cannot be overstressed. It may sound trite to say that material for biopsy must contain cancer before cancer can be revealed under the microscope. Most pathologists can testify to personal experience with tissue submitted to them from cancer-afflicted patients which either showed no cancer or was of debatable character while full-blown carcinoma existed a few millimeters from the site of the specimen. Tissue removed from a small circumscribed area suggestive of cancer should include both material from the suspicious area and a generous amount of adjoining normal-appearing tissue. The block so obtained should be rectangular or nearly so, as shown in the accompanying illustration, and should immediately be fixed in solution of formaldehyde or other suitable fixing solution. If the material is obtained and prepared in this way, when it is ready for microsectioning there is little doubt about the direction in which the block should be cut. Minute fragments of tissue, wedge-shaped pieces of tissue and material obtained by scooping out tissue with the endothermy loop may be entirely unsatisfactory. The advisability of curetting the surface of the process as has been recommended is also a dubious procedure. Ordinarily there can be little excuse for such haphazard methods when the lesion is small, circumscribed and primarily a diagnostic problem.

When the area under suspicion is more diffuse or located on a cervix that otherwise merits some form of operative correction, an amputation or a Sturmdorf procedure combined with amputation, as described by Te Linde,[1] is a convenient method of simultaneously obtaining material for biopsy and correcting a local pathologic condition. Whether the scalpel or the endothermy current is employed for this purpose probably matters little. However, if the latter is used one should allow for destruction by heat along the margins, where the fragment of tissue becomes unsuitable for histologic study. When a tumor is large and its character obvious, naturally observance of such minutiae is not essential.

One must of course recognize that early visible cancer probably has no distinctive gross appearance which permits its exact clinical diagnosis. Heretical as it may sound, it is also probably true that more advanced cancer possesses no distinctive or grossly pathognostic appearance. Its clinical recognition rests on the fortuitous circumstance that most ulcerating, indurated tumors of the portio are cancer.

Aside from such relatively rare lesions as those of syphilis, tuberculosis and venereal granuloma, all of which may grossly simulate cancer, the lesion which according to my experience is most commonly suspected of being an early cancer is the vermilion zone so commonly observed about the external os. This, generally referred to as an "erosion" or "ulceration," has a well marked tendency to bleed when complicated by vaginal inflammation, which renders the red surface especially susceptible to slight trauma, with the production of minute bleeding points (erosions). Generally, however, the circumostial vermilion zone does not bleed and does not partake of the nature of erosion or ulcer.

The differentiation of a circumostial vermilion zone of altered epithelization from an established cancer of similar size should ordinarily not be difficult. The former may be relatively smooth and flat or it may possess a fine irregularity giving it a finely granular appearance. It does not, however, appreciably change the gross contour of the cervix. If it involves both lips of the cervix, as it often does, it has its greatest expanse on the anterior and posterior lips, with narrow lateral connecting zones of red. On palpation with a sound the surfaces are found to be elastic, and under magnification cervical glands are visible pouring forth their watery secretion onto an intact, red and glistening mucosa.

1. Te Linde, R. W.: Amputation of the Cervix with Application of the Sturmdorf Flap Principle, Surg., Gynec. & Obst. **43**: 513 (Oct.) 1926.

A small carcinoma on the surface of the portio does not have as perfect a circumostial distribution as the common vermilion zone does, and ordinarily it is elevated, so that it alters the contour of the cervix. Its color generally offers a distinct contrast to the surrounding mucosa, while its surface is generally irregular and may show the opening of cervical glands. Palpation of the tumor with a sound reveals the irregularity previously noted and a lack of elasticity, and if there is beginning degeneration of the tumor the sound can be pushed with little force into the substance of the tumor, which then bleeds readily.

A small cancer with ulceration can so simulate a benign, nonspecific, inflammatory process of the cervix, while a benign process when complicated by induration and bleeding can so mimic cancer, that their gross differentiation may be impossible. However, such instances have so far been relatively uncommon.

Summarily, then, early cancer of the vaginal portion of the cervix that is clinically recognizable, as ordinarily encountered, presents a gross appearance which shows sufficient deviation from the normal to arouse suspicion. Obviously its true nature may not be recognized. Nevertheless, thoughtful appraisal of the lesion on the first examination should arouse sufficient concern to stimulate the proper removal of tissue for histologic study.

COVERT CANCER

I come now to a consideration of those processes on the vaginal portion of the cervix which, though their appearance does not correspond to the customary gross appearance of cancer, may represent an early phase of malignant change, i. e. covert cancer. Until comparatively recently such processes have been detected accidentally, on laboratory examination and have been unrecognized clinically as either potential or bona fide early nonulcerating cancer.

The ability to recognize clinically such processes represents a sort of cancer utopia which has probably been the dream of every physician at some stage of his medical career and is still the goal of many students of cancer.

The question is Have physicians reached this goal? The attempt has been made to bridge the hiatus between the phase of early tumefaction and ulceration of cancer and the antecedent covert stage, in which these changes have not occurred.

Presumably cancer of the portio vaginalis cervicis in its incipience passes through a stage in which the cells of the stratified epithelium in a localized area possess all the histologic earmarks of cancer but lack the property of invasion. I prefer to term this carcinomatoid process, limited to the normal boundaries of the epithelial zone before it has proved its destructive ability, probable beginning cervical cancer, because the expression carries a connotation of doubt. Such processes are also designated superficial cancer, cancer in situ, Bowen's disease, and carcinoid change. The term "precancerous" if ever permissible might conceivably also be used. The word, however, has such a definitive connotation that, with our present limited knowledge of cancer, it is doubtful that it can justifiably be employed.

Laying aside all theoretic considerations, one cannot say positively whether the ultimate fate of such suspicious lesions will be one of steady progression to invasion and full-blown malignancy or whether there may occur a process of regression and restitution to normal. Similar epithelial changes are occasionally found at the periphery of bona fide cancers, and it is therefore necessary when the histologic picture of probable beginning cancer is seen to make certain that the material has not come from the margin of a full-blown malignant process.

Attention has been focused on these controversial areas of probable beginning cancer by the efforts of Hinselmann [2] and of Schiller.[3]

In the opinion of some authorities it is now possible to recognize clinically such early manifestations of presumptive cancer before the process of ulceration and prior, consequently, to the production of abnormal vaginal discharge, which is dependent on this change. The clinical methods designed to bring to one's attention areas of early covert cancer are limited in their application to the vaginal portion of the cervix uteri. The iodine test was proposed by Schiller, while Hinselmann advocated observation of the cervix under magnification with a suitably mounted binocular dissecting prism, which he has termed a colposcope.

The rationale underlying the iodine test of the epithelium of the vaginal portion of the cervix as proposed by Schiller is based on the observation of Warburg that cancer cells possess a higher sugar metabolism (glycolysis) than normal epithelium and the observation by Lahm, Schiller and others that cancerous epithelium usually shows an absence of glycogen. Since it has been shown by Langhans that iodine reacts with glycogen in living tissue the iodine test has been applied clinically to reveal areas possessing or lacking glycogen. The test, which has been given rather general use, is done simply by applying iodine in the form of Gram's [4] iodine solution to the cervix, which has been cleansed of its secretion. Normal mucosa assumes a mahogany brown color of varying intensity after from five to ten seconds of constant application. The iodine solution should be comparatively fresh.

THE COLPOSCOPE

The colposcope was devised by Hinselmann as a result of his observation of two large areas of leukoplakia (white plaques) on the vaginal portion of the cervix. Histologically these areas showed the cellular changes ascribed to cancer (mitoses, irregularity in size, shape, relationship and staining reaction of the cells) but they were limited to the anatomic confines of the epithelial zone, i. e. invasion was lacking. On the basis of this observation and a few earlier observations by von Franqué and others, which I [5] have discussed elsewhere, it appeared reasonable to infer that leukoplakia offered a starting point for cancer. Indeed, it has long been held by von Franqué [6] that cancer of the portio probably manifests itself first as a leukoplakic change and conversely that certain leukoplakic plaques are

2. Hinselmann, H.: Zur Kenntnis der präcancerosen Veränderung des Portio, Zentralbl. f. Gynäk. **51**: 901-903 (April 9) 1927.

3. Schiller, W.: Untersuchungen zur Entstehung der Geschwülste: Collumcarcinom des Uterus, Virchows Arch. f. path. Anat. **263**: 279-367, 1927; Zur klinischen Frühdiagnose des Portiokarzinoms, Zentralbl. f. Gynäk. **52**: 1886-1892 (July 28) 1928.

4. Confusion exists regarding the type of iodine solution advised by Schiller. Since he referred to Lugol's solution in his original communication, it has been inferred by some workers that Lugol's solution as defined in the U. S. Pharmacopeia (compound solution of iodine U. S. P.) was meant. Schiller's reference, however, was to Lugol's solution as used for bacterial stain, which is the equivalent of our Gram's iodine solution (iodine 1 part, potassium iodide 2 parts, water 300).

5. Martzloff, K. H.: Leukoplakia of the Cervix Uteri: A Manifestation of Early Malignant Change? Am. J. Obst. & Gynec. **24**: 57 (July) 1932.

6. von Franqué, O.: Leukoplakie und präcanceröse Veränderung des Plattenepithels, Zentralbl. f. Gynäk. **51**: 898 (April 9) 1927.

destined eventually to become cancers. It therefore appeared logical to attempt to recognize these changes in their incipience, when they might be so small as to escape observation by the unaided eye. The magnification of from 10 to 15 diameters which the colposcope provides is designed to make such recognition possible and also to permit study of lesions other than leukoplakia.

Study of the cervix under magnification is interesting and informative if one controls one's observations with histologic studies. One learns that the cervix generally has a slight but definite pulsation synchronous with the heart beat; that cervical glands may open onto the portio 1 or 2 cm. from the external os through a normal stratified epithelium, which is bathed by their intermittent, crystal-clear secretion, and that glandular openings commonly occur also in the circumostial vermilion zone and may have there small yellowish gray plugs simulating leukoplakia. Also it is not uncommon to note at the transition zone, where the pale pink of the normal stratified epithelium meets the bright red of the thin epithelium of the vermilion zone, areas where the epithelium is pale gray, almost white. Minute bleeding points (erosions) and small ulcers can be readily identified, as can also other more major deviations from the normal.

RESULTS OF TESTS

The question naturally arises as to how valuable these two methods are for the recognition of incipient cancer when compared with ordinary methods of careful inspection.

My experience with these methods now extends over approximately seven and one-half years. Unquestionably the iodine test is not specific for cancer or for areas of so-called probable beginning cancer. Schiller originally pointed out some of the pitfalls in this test but felt that nonstaining areas are often though not always cancerous. According to my experience the overwhelming majority of unstained areas, including areas of leukoplakia, show no histologic evidence suggestive of probable beginning cancer. Small epithelial gland plugs, vermilion areas, a proportion of superficially situated nabothian follicle cysts, areas of epithelial loss, either when superficial or, if complete, apparently when fibrin covers the base of the ulcer, epithelium involved in an underlying inflammatory process and particles of adherent inspissated secretion, together with other unexplained areas, fail to stain with the iodine. It follows that if areas that do not stain with iodine are not interpreted with due reserve they lead to endless confusion and alarm for the physician and unnecessary biopsy, cervical tinkering and hysteria for the patient.

Up to the present time I have not discovered a histologically proved area of probable beginning cancer with the iodine test, nor has the test proved to be of any more assistance than careful inspection with the unaided eye.

The altered epithelium that does not stain with iodine which occurs at the periphery of some established carcinomas has, as in Henriksen's case,[7] occasionally led to the suspicion and recognition of a cancer. So far, however, in most of such published instances[8] there was a history of bleeding and an ulcerating cancer was present which should have been suspected from the beginning. It is, I believe, permissible to conclude that in its general application a test as unspecific as the negative iodine reaction is likely to be more confusing than it is to be helpful. Certainly, as I have noted elsewhere,[9] the test is not pathognomonic of a malignant condition, though it may possibly be a signal which calls for further study.

The colposcope, since it facilitates visual observation of the cervix uteri, would naturally appear to answer an unfulfilled need and to fall into the category of nasal and aural speculums, the proctoscope and the cystoscope. However, the corollary is not as apt as it sounds, for from the standpoint of the profession at large it has several drawbacks which probably will prevent its general adoption. These include the expense of the instrument, the time necessary to make a careful study and the need of extended experience to interpret correctly what one sees. The need of extended experience makes it necessary for the clinician to use the instrument regularly and to correlate the colposcopic appearance of the cervix with the histologic picture of the area in question. This requires frequent biopsies and study of the tissue by the clinician himself. The obtaining of tissue for biopsy takes the method out of the realm of simple office procedure, for if an area is sufficiently abnormal in appearance to warrant removal of tissue, removal should be carried out as described earlier in my discussion. An inadequate specimen for biopsy is probably worse than none, for it frequently makes it impossible for the pathologist to arrive at a correct interpretation. If cancer is present and the specimen does not contain any of it the patient's welfare is unjustifiably jeopardized.

However, I believe that the colposcope is a fundamental contribution to methods of visual examination of the vaginal portion of the cervix uteri. While I use it as a routine, it has been of essential value in only a few instances. So far I have discovered with it neither areas of unmistakable probable beginning cancer nor any small cancerous ulcers (established cancer) which I could not detect with the unaided eye on careful methodical examination. It is important to appreciate fully that the gross appearance of the small lesion of early established cancer, as pointed out by Hinselmann,[10] is not sufficiently characteristic to permit its differentiation from other nonmalignant lesions solely on the basis of its appearance through the colposcope.

EXPERIENCE OF VARIOUS WRITERS

A review of the more recent literature reveals a decided division of opinion, the details of which cannot be discussed here. Of fundamental importance, however, are the following observations: 1. Claims that leukoplakia of the cervix uteri is a precursor of cancer[10] lack confirmation at this time.[11] 2. Many of the histologic diagnoses of cancer made by Hinselmann have not been confirmed by disinterested pathologists to whom sections were submitted,[12] and there is no proof

7. Henriksen, Erle: Precancerous and Carcinoid Lesions of the Cervix Uteri; with Comments on the Schiller Test, Surg. Gynec. & Obst. **60**: 635 (March) 1935.

8. Graves, W. P.: The Detection of the Clinically Latent Cancer of the Cervix, Surg., Gynec. & Obst. **56**: 317 (Feb.) 1933.

9. Martzloff, K. H.: Recognition of Early Cancer of the Cervix Uteri, Internat. Clin. **4**: 179 (Dec.) 1934; Early Cancer of the Cervix Uteri: The Practicability of Its Recognition Before the Stage of Ulceration, Northwest Med. **34**: 295 (Aug.) 1935.

10. Hinselmann, H.: Die klinische und mikroskopische Frühdiagnose, Arch. f. Gynäk. **156**: 239, 1933.

11. Schiller, Walter: Leukoplakia, Leucokeratosis and Carcinoma of the Cervix, Am. J. Obst. & Gynec. **35**: 17 (Jan.) 1938. Borst, in discussion on Hinselmann.[10]

12. Winter, G.: Das Kolposkop bei der Krebsbekämpfung, Zentralbl. f. Gynäk. **61**: 2147 (Sept. 11) 1937.

at this time, as has been claimed,[13] that 20 per cent of areas of leukoplakia that are studied are carcinomatous. 3. Some of the cases reported to show the value of the colposcope for revealing an otherwise unrecognizable early cancer are reasonably debatable from the standpoint of their acceptability. If, for example, cancer is present it may be impossible to ascertain from the case report which part of the gross lesion showed cancer,[14] and, in fact, the proof of cancer may not be clear.[15] In the case reported by Leip and Otto,[16] in which leukoplakia presumably of twelve years' standing under constant observation underwent bona fide cancerous change, the patient in question was not seen by the authors until a few months prior to the time of her operation, and two years prior to this her cervix had been considered suggestive of cancer and biopsy had been advised on the basis of a speculum examination without a colposcope. 4. The infrequency with which cancer is found on routine prophylactic examination is evident from the experience of Hinselmann and Köhler.[17] These authors examined 1,133 women in three and one third years in the municipal woman's clinic of Altona. These women represented a special group who were without other complaint and either sought examination for cancer prophylaxis (sixty-eight instances) or had been referred by other physicians for this particular type of examination because of a "suspicious" cervix. Sixteen women (1.4 per cent) of this entire highly selective group showed histologic evidence of so-called probable beginning cancer. Obviously no such incidence would occur in an unselected group of women who were similarly examined.

COMMENT

One cannot escape the feeling that there is considerable partisanship and bias on the part of the proponents of the colposcope. In fact one sees the question raised, in some of the discussions, of the advisability of enacting legislation compelling physicians who examine patients under the existing German sickness insurance plans to use the colposcope in all vaginal examinations.

The impression is unescapable that for the present the recognition of cancer of the cervix uteri in its early stages still rests on painstaking visualization and inspection and proper obtainment from unusual appearing areas of tissue for microscopic examination. To await the appearance of a large ulcer formation, obvious induration or a cauliflower-like tumefaction such as that described in textbooks before clinically suspecting cancer is like preparing for sea after the ship has sailed.

This critical evaluation of methods more or less recently popularized for the apparent simplification and ready determination of early cervical cancer should not be construed as unfriendly criticism. However, as noted before, on the basis of a fairly long and appreciable experience I believe that these methods possess greater limitations than is ordinarily ascribed to them. If these restrictions are appreciated, one will not be discouraged by finding little where much was anticipated.

808 Medical Dental Building.

13. Hinselmann, H.: Die Grundlagen der kolposkopischen Karzinombekämpfung, Zentralbl. f. Gynäk. **58**: 2798 (Nov. 24) 1934.
14. Mestwerdt, Gustav: Zur Frage der Diagnose des latenten Portiokarzinoms, Zentralbl. f. Gynak. **61**: 2742 (Nov. 27) 1937.
15. Mönkeberg, Agnete: Auch ein Anfanger kann das Portiokarzinoms im ersten Beginn mit dem Kolposcop endecken, Zentralbl. f. Gynäk. **62**: 52 (Jan. 1) 1938.
16. Leip, F., und Otto, Karl: Ein Portiokarzinom, entstanden aus einer 12 Jahre lang beobachteten Leukoplakie, Zentralbl. f. Gynäk. **61**: 242, 1937.
17. Hinselmann, H., and Köhler: 3½ Jahre "Krebssprechstunde" mit dem Kolposkop, München. med. Wchnschr. **84**: 1082 (July 9) 1937.

Council on Industrial Health

ETIOLOGY OF PNEUMOCONIOSIS

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This paper is one of a series on pneumoconiosis prepared at the request of the Council on Industrial Health. The succeeding articles will be published when available.—ED.

Although the term pneumoconiosis was not introduced until the nineteenth century, clinical symptoms were naturally enough associated with the inhalation of dust in occupation by the earliest medical writers. In the Renaissance both physicians and mining engineers were well aware of the fact that the metal miner suffered from shortness of breath and died prematurely, and anatomists had described "heaps of sand" in the lungs of stone cutters which grated on their knives. They called the condition phthisis, their term for any chronic disease of the lungs which was associated with emaciation and expectoration. While most of the various conditions originally known by this name were differentiated and fully described in the eighteenth and nineteenth centuries, it was not until 1902 that the role of inhaled dust began to be understood. In that year an English departmental committee, of which Dr. J. S. Haldane was the outstanding member, pointed out that the phthisis from which the Cornish tin miners suffered was different from ordinary tuberculosis. They concluded that "the primary injury of the lungs is due solely to the inhalation of stone dust but that this injury, while it is apparently capable of gradually producing by itself great impairment of respiratory functions . . . also predisposes enormously to tuberculosis of the lungs, so that a large proportion of the miners die from tubercular phthisis."

A few years later, in 1915, Collis[1] demonstrated that not all kinds of dust had the same effect. His statistical analyses of morbidity and mortality in workmen in various dusty trades indicated most clearly that exposure only to free silica dust was particularly dangerous. Such exposure caused disability with ultimate death from tuberculosis at an age period later than occurred in the rest of the population. Inhalation of silica combined as silicates or of nonsiliceous dusts had no such effects. Collis felt very strongly that the free silica particles did not injure the lungs by virtue of their hardness and sharpness because other particles with the same properties failed to do so, but he could offer no other explanation. In 1922 Gye, Kettle and Purdy[2] demonstrated that colloidal silica is toxic for rabbits and suggested that crystalline silica is dissolved in the body to produce the toxic colloid. These contributions of Collis and of Gye, Kettle and Purdy still dominate modern concepts of pneumoconiosis.

Clinical research in South Africa under the leadership of Watkins-Pitchford and Irvine clarified the relationships existing between the reaction to inhaled silica and tuberculous infection. By employing the method of serial roentgenography over long periods of time and checking their observations with post-

From the Saranac Laboratory for the Study of Tuberculosis of the Edward L. Trudeau Foundation.

1. Collis, E. L.: Industrial Pneumoconiosis, with Especial Reference to Dust Phthisis, Milroy Lectures, 1915, Pub. Health **28**: 252-292, 1915.
2. Gye, W. E., and Purdy, E. H.: The Poisonous Properties of Colloidal Silica, Brit. J. Exper. Path. **3**: 75-85 (April) 1922. Gye, W. E., and Kettle, E. H.: Silicosis and Miners' Phthisis, ibid. **3**: 241-251 (Oct.) 1922.

mortem examinations these observers have probably contributed more than any other group to a sound understanding of the pathogenesis and pathology of silicosis. Their work established the dual relationship existing between the infectious process tuberculosis and silicotic fibrosis. The infection may on the one hand remain latent and exert only an etiologic effect in modifying the amount and form of the reaction to silica dust; on the other it may itself develop in active but unusually chronic form as a result of the preestablished silicosis.

Until 1924 Collis's dictum that only free silica is a cause of pulmonary fibrosis remained unchallenged. In that year Cooke [3] reported a case in which inhaled asbestos was incriminated; other cases were soon discovered and today asbestosis is everywhere recognized as a second form of pneumoconiosis characterized by fibrosis. The disease can apparently be produced by the prolonged inhalation of any of the five different silicates known as asbestos. This form of pneumoconiosis does not seem to predispose to tuberculosis to the same degree as silicosis. Although English authorities believe that it has considerable effect, American experience has failed to reveal an excess of tuberculosis among asbestos workers.

A few years later Badham [4] reported peculiar conditions found on roentgen examination in a large group of gold miners in Western Australia. These men had been exposed to a dust containing a small amount of quartz mixed with a silicate of magnesium known as rhodonite. Since Badham's films bore a certain resemblance to those showing asbestosis and to those of men exposed to various other silicate dusts, he proposed the term "silicatosis" to describe all these conditions. His proposal has not been generally accepted as proof that the silicates as a class can produce fibrosis.

Today Collis's clearly defined concepts of pneumoconiosis are becoming confused again because enthusiastic observers in many fields are drawing deductions without sufficient knowledge of the problem as a whole. Roentgenologists are too ready to ascribe any abnormal shadow in the film of a workman to some dust which he may have inhaled. General pathologists have concluded that the mere presence of a certain mineral in a pulmonary lesion is *ipso facto* proof that this dust was the cause of the reaction. Experimental pathologists with high powered microscopes have searched the early reactions to inhaled dusts and drawn sweeping conclusions as to the potentialities of this or that mineral to cause fibrosis. Petrologists and chemists are performing test tube experiments which prove that some silicate is more soluble in water than quartz, deducing from the solubility hypothesis that it must therefore be a more potent irritant than quartz. Clinicians, who see only the disabled silicotic patient with advanced lesions, often complicated by tuberculosis, are insisting that only such conditions represent the true picture of silicosis.

Such intensive research on the different aspects of the problem is yielding valuable information, but theoretical knowledge is not yet sufficiently advanced to permit an evaluation of a hazard by mere analysis of dust or rock. At the present time the detailed study of the workman and his industrial environment still constitutes the only certain method of establishing the existence of a dust hazard. Such investigations are profitably based on the experience of the Miners' Phthisis Prevention Committee in South Africa. They should include the following:

1. The occupational history of all employees should cover the entire industrial life of every workman. It should include the names of each employer, the kind of job, an estimate of the type and quantity of dust encountered and the approximate dates of each position held. The information is apt to be recalled most readily in reverse chronologic order.

2. Roentgenologic examination of the chest constitutes the most important source of information as to the presence of abnormal changes in the lungs. For the detection of advanced lesions almost any quality of roentgenogram on film or paper will suffice; to discover early changes the best stereoroentgenograms are none too good. The interpretation of the films presupposes a thorough knowledge of the normal pulmonary patterns, a familiarity with the shadows of infectious lesions, and judgment unbiased by the knowledge that the subject may have been exposed to considerable dust.

3. Physical examination of the chest is of equal significance. In many cases in which films may reveal widespread pneumoconiosis, even of a silicotic type, the physical signs will be very slight, but this paradox in itself is significant. Complicating infections are usually productive of characteristic signs but they are often less obvious than in cases of simple infection. Only by physical examination is it possible to evaluate the effect of the pulmonary condition and determine whether disability exists.

To be most profitable, such examinations should be repeated at intervals, annually if possible and on infected individuals as often as the examining physician deems necessary. By serial reexamination of a considerable group it is possible to obtain an idea of the pathogenesis of a pneumoconiosis, its rate of development and its extent and probable outcome. Isolated examinations, not repeated, demonstrate the prevalence of abnormal changes in the lungs of the workmen. Little information as to evolution of disease can be obtained for the conditions of exposure in the present, and previous employment varies with the individual workman.

4. Postmortem examination of the lungs should be made as frequently as possible. Careful gross and histologic study of the pulmonary lesions constitutes the best guide to the interpretation of the shadows which are cast on a roentgenogram. Chemical and petrographic analysis of the lungs determine the amount and character of the inhaled mineral dust. The larger the number of such postmortem examinations the greater the likelihood of formulating a true concept of the disease arising from the dust under investigation. One or two isolated examinations may only obscure the picture because of previous exposures to other dusts not accounted for in the occupational history.

5. A detailed study of the industrial environment includes a chemical and petrographic analysis of the raw materials, in the case of a mine of the ore and the rock being worked, of a grinding operation of the wheels and the implements ground, and so on. But it should not be assumed that the composition of the raw materials will necessarily correspond with that of the dust created by manipulating them. It will be shown later that the free silica content of the rock may greatly exceed that of the dust liberated from it. Likewise, samples of dust settled on rafters do not necessarily contain the same proportion of silica as the dust suspended in the atmosphere. Analysis of air-floating material at the breathing level constitutes the only accurate measure of the dangerous minerals that a workman is likely to inhale. The relative amounts of silica and all other minerals should be determined because of mutual interactions which may reduce the concentration of the silica or modify its effects on the body. Not only the kind but

3. Cooke, W. E.: Fibrosis of the Lungs Due to the Inhalation of Asbestos Dust, Brit. M. J. **2**: 147 (July 26) 1924.

4. Badham, C.: Notes on a Fine Type of Fibrous Pneumoconiosis Produced by Silicates and Other Minerals, Report of Director-General of Public Health (New South Wales) for year ended Dec. 31, 1927, Sydney, Australia, Government Printing Office, 1929.

the quantity of the atmospheric dust must be measured. In the United States the Greenburg-Smith impinger apparatus is the standard, and the results are expressed in millions of particles per cubic foot of air. Other instruments, such as the Kotze konimeter used in South Africa, the Owens jet counter in Great Britain and the Bausch and Lomb dust counter in this country, give equally satisfactory results but ones which are not reciprocally translatable.

Such determinations must be made in all the various parts of the plant or mine where men are at work, for both the quantity and the quality of the dust vary from the point of generation to others more remote. Furthermore, repeated sampling is essential to establish the amount of dust that the men inhale in any operation. Local variations in the velocity of air, humidity and general ventilation all affect the picture. The average amount of atmospheric dust must be based on many samples taken over periods of months or years.

By correlating the results obtained from such a study it is possible to evaluate the effects of the particular dust under the conditions existing in a particular plant. The results can be applied to another industry only when it has been proved that the composition and concentrations of dust in the second plant are similar. Only then is it safe to assume that the mass effects will be comparable. Individual variations will always be discovered because certain persons are more susceptible to dust by virtue of associated pulmonary infections. Sometimes the picture in the whole group will be altered because of a high local incidence of tuberculosis.

EXPERIMENTAL INVESTIGATIONS

Since so many industrial processes involve creation of dust and since a detailed study of each one of them would be both time consuming and expensive, there is reason to seek accessory sources of information. Animal experimentation has demonstrated its value as such a source. While many experiments have failed to reproduce disease processes entirely comparable to those observed in human beings, they have demonstrated fundamental principles which govern the reaction of living tissues to various kinds of mineral particles.

The experimental pathologist may test the action of a given dust by the inhalation method, which purports to create an atmospheric environment comparable to that in industry. This method is time consuming, expensive and fraught with technical difficulties, and frequently it fails to produce the anticipated results. The experimenter sets up rigidly controlled conditions, which are kept as constant as possible over periods of months or years; in industry conditions are rarely constant but continue to change from hour to hour. With pure mineral dusts experimental inhalation generally produces a pneumoconiosis comparable to that in human beings. With dusts composed of mixtures of silica and other minerals the results are often disappointing even when the dust being tested is the apparent cause of human disease. Failure may be due to the time limitation imposed by the span of life of the ordinary laboratory animals or by the failure to appreciate and reproduce the complex factors of industrial exposure. Nevertheless the inhalation method may lead to an appreciation of these factors; it is establishing the conditions which govern the behavior of atmospheric suspensions of dust particles and those which determine inhalation into the lungs. It is elucidating the pathogenesis of various pneumoconioses in normal and in infected lungs.

By injection methods the experimenter may demonstrate the potentialities of any type of mineral to irritate living tissues and may determine the character of the response. He must avoid technics which produce confusing nonspecific effects due to local trauma and the mere mechanical action of large amounts of any foreign body. This objection can be overcome by injecting dilute suspensions of particles at points remote from the site of ultimate localization. I prefer repeated intravenous injections of dilute suspensions of particles which permit gradual accumulation of the test substance in different organs. I have also employed the Miller-Sayers [5] intraperitoneal method; this gives good gross reactions but the microscopic pictures are hard to evaluate. Experiments with intratesticular injections are also in progress and may prove useful.

Since the objective is the determination of the capacity of a mineral to cause fibrosis, it generally makes very little difference whether its action is tested in the lung or in some other organ. Fibrous tissue develops from continued stimulation of connective tissue cells regardless of their location. As far as is known, these elements are just as capable of stimulation in the spleen or liver as in the lungs. In the case of free silica, this assumption has been proved beyond question, and furthermore it has been shown to hold good in any species of animal tested. The only apparent exceptions thus far discovered have been the fibrous minerals known as asbestos, which have produced little or no scar tissue outside the lungs. Reasons will be cited for suspecting that the fibrosis of asbestosis is due to mechanical irritation which is restricted to the lungs because of the active motion of this organ. In other locations the factor of rapid and continuous motion is lacking.

The etiology of the pneumoconioses will be discussed first from the point of view of the capacity of different minerals to irritate the tissues; the factors that govern the behavior of air-borne dust will then be considered, and finally the host factors that determine the amount of dust inhaled and modify the cellular reactions. For this consideration the minerals will be classified into groups consisting of free silica, combined silica, nonsiliceous particles and mixtures composed of free silica and other substances.

A recent paper [6] reported uncompleted results of injections of physiologic solution of sodium chloride suspensions of different mineral particles into animals. These are summarized in tables taken from that publication but brought up to date when longer periods of observation have supervened. The capacity of different mineral particles of the same size and concentration to irritate the tissues is indicated by a series of numerals and plus signs. The significance of these symbols is indicated by the following definitions:

± Simple phagocytosis, often by giant cells, without other cellular reaction; no fibrosis.

+ Phagocytosis plus small localized collections of lymphocytes; reaction nonprogressive; no fibrosis.

2+ Similar to + but with more extensive infiltration of lymphoid cells; reaction nonprogressive; no fibrosis.

3+ Early proliferation of mononuclear cells, localized to immediate vicinity of primary phagocytes with further evidence of chronic inflammation. If any elements of fibrosis appear they are microscopic in extent and nonprogressive in character.

5. Miller, J. W., and Sayers, R. R.: The Physiological Response of the Peritoneal Tissue to Dusts Introduced as Foreign Bodies, Pub. Health Rep. **49**: 80-89 (Jan. 19) 1934.

6. Gardner, L. U.: Reaction of the Living Body to Different Types of Mineral Dusts With and Without Complicating Infection, Mining Technology, May 1938.

4+ More extensive proliferation followed by fibrosis suggestive of early silicosis but not progressing to the mature hyaline stage.

5+ Typical, nodular, silicotic fibrosis, hyaline in character and progressive in type; the standard reaction.

6+ and 7+ Progressive fibrosis, hyaline in character but diffuse rather than nodular in form; observed only with two synthetic forms of free silica, crystobalite and tridymite.

8+ Acute toxic reactions with local necrosis of cells often resulting in death of the animal; little fibrosis in event of survival.

FREE SILICA

Table 1 sets forth the forms of free silica which have been tested by intravenous injection of 1 Gm. of particles of from 1 to 3 microns in diameter into the ear veins of rabbits and by other methods. The maximum period of observation in all cases has been eighteen or twenty-four months.

It will be noted that all the crystalline and cryptocrystalline forms of free silica are as active as or more active than the standard normal quartz. All of them have also produced progressive fibrosis of a silicotic type in guinea pigs, rabbits and white rats and in some cases other species. These results indicate that all the forms of free silica enumerated are capable of producing a progressive fibrosis if effective quantities remain in contact with living connective tissue. They prove nothing as to the capacity of these forms of silica to remain suspended in the atmosphere and to be inhaled in dangerous quantities.

TABLE 1.—*Free Silica*

Crystalline Forms		Cryptocrystalline Forms		Amorphous Forms	
Normal quartz	5+	Chalcedony	5+	Colloidal silica, dispersed	8+
Tridymite	7+	Tripoli (Seneca, Mo.)	5+	Colloidal silica, gel	±
Crystobalite	6+	Flint	5+	Opal	4+
Vitreous silica	5+			Diatomite	5+

The observations on the amorphous varieties of free silica are more variable. Colloidal silica in a dispersed phase is exceedingly irritating and in too large an intravenous dose it causes almost immediate death. If the same suspension is allowed to gel either spontaneously or by changing its reaction, the silica promptly loses its irritating properties. The finely ground particles of the gel are phagocytosed by mononuclear cells, which subsequently develop epithelioid characteristics and often form giant cells of the Langhans type.[7] But with these transformations in the primary phagocyte, the manifestations of irritation cease; there is not even a local infiltration with lymphocytes to suggest any effect on the surrounding tissues. The picture has remained unchanged over a two year period; if anything the number of giant phagocytes has been less in animals killed two years after injection than in one killed at three months.

The natural minerals composed of amorphous silica, like opal and diatomaceous earth, are much more active. Pure diatomite produced a reaction which was indistinguishable from that to quartz, while opal caused a nonhyaline fibrosis which was atypical and which had begun to retrogress after a period of one year. In an attempt to explain this puzzling difference in the irritating properties of different forms of free amorphous silica, supplementary tests are being made with synthetic gels of variable water content. Eight months after injection into the peritoneal cavities of guinea pigs not one of the six compounds has produced any appreciable fibrosis. The factor of water content can in all probability be eliminated. The desirability of testing other natural forms of amorphous silica is obvious.

Further supplementary tests have revealed pertinent facts with regard to the behavior of normal quartz and the other crystalline forms. The factor of dosage will be of more importance when the effects of mixed dusts are discussed. For pure, free, active silica the dose employed in all these tests has been excessive. As little as 0.05 Gm. of normal quartz will cause as much reaction as 1 Gm. in a 5 pound (2.3 Kg.) rabbit, but two years instead of one is required for mature reaction. A dose of 0.01 Gm. causes no visceral fibrosis, but the lymph nodes are still involved (the result of lymphatic drainage). Nevertheless the 1 Gm. dose has been used for the comparative study to insure the presence of adequate quantities of minerals that may be less irritating than quartz.

The rate and extent of tissue reaction are inversely proportional to particle size.[8] When the quartz is larger than 10 microns in diameter, reaction does not progress appreciably during a two year period of observation. Particles less than 1 micron in diameter cause increasingly acute inflammatory responses and often death from hepatic insufficiency within a few months. However, the size can be reduced to a point such that the particles are no longer retained in most parts of the body, and then their effect is again negligible. Intravenous injection of 1 Gm. of active vitreous silica particles with a maximum diameter of 0.002 micron produced no symptoms, but excessive amounts of silica were present in the urine. All the animals survived and when they were killed showed only minute foci of silicotic fibrosis.

Inhalation tests were also attempted with this fine dust to determine whether appreciable quantities would be retained in the lungs. The exposure to an undefined concentration of this very fine dust was continued for eight hours daily over a period of five months. At the end of this period pneumonia was making heavy inroads into the group, probably because of overcrowding in too small a dusting chamber. When the survivors were killed their lungs showed no fibrosis, but giant cells of the Langhans type were even more numerous than with larger quartz. It was concluded that some of the fine silica was retained, but in the absence of a method of measuring the atmospheric concentration the amount could not be estimated.

SILICATES

In a similar manner a group of representative silicates, most of which are used in industry, are being subjected to tests by animal injection. Table 2 summarizes the results as far as the observations have progressed. Not included in the table is a series of tests on synthetic sodium silicate. This substance is exceedingly toxic when the standard dose of 200 mg. is injected into the peritoneal cavity of guinea pigs. The animals die within a few minutes, exhibiting symptoms of silicic acid poisoning. Presumably its ready solubility is responsible for the toxicity of this silicate. Incidentally, repeated injections of minute quantities of the same substance into the lungs have

7. Gardner, L. U.: The Similarity of the Lesions Produced by Silica and by the Tubercle Bacillus, Am. J. Path. **13**: 13-23 (Jan.) 1937.

8. Gardner, L. U., and Cummings, D. E.: Reaction to Fine and Medium Sized Quartz and Aluminum Oxide Particles: Silicotic Cirrhosis of the Liver, Am. J. Path. (supp.) **9**: 751-763, 1933.

caused neither symptoms nor fibrosis, so that it seems fair to conclude that any quantity of sodium silicate which could be inhaled would be harmless.

As far as these observations have progressed, none of the silicates have proved capable of producing a fibrous type of reaction. Some of them, marked "(d)" in the table, have caused sudden deaths on intravenous injection into rabbits. Such reactions, owing either to mechanical occlusion of the blood vessels or to the toxic action of silicic acid formed in the preparation of the dust suspensions, probably have little to do with the subject under discussion. Beryl is apparently toxic and produces acute local inflammation that invariably leads to death. A few of the silicates, notably biotite mica and some of the clays, have provoked local proliferation of mononuclear phagocytes. Whether this early reaction will ultimately end in fibrosis awaits demonstration. If fibrosis should develop it will do so only after much longer contact with the tissues than is required in the case of free silica. Most of the silicates have excited an inert foreign body type of tissue response consisting of simple phagocytosis and giant cell formation with or without lymphocytic infiltration. Such reactions either have remained unchanged for periods of one or two years or have tended to retrogress. It is of interest to note that fibrous sericite of the type which Jones [9] stated might be such an important adjunct in the production of silicosis is among the most inert of the silicates.

Since the first publication on the action of silicates [6] the results of a few tests by still other methods have become available, which suggests that these tentative conclusions may need revision. When 5 mg. of suspensions of several different minerals was injected directly into the testes of guinea pigs it was found that the same feldspar produced a very active cellular proliferation within six months. Talc produced a less active response of a similar character. Garnet, sillimanite and platy sericite behaved in just the same manner as they did in the tests previously reported. The intratesticular injections involved excessive local concentrations, but the marked difference between the response to several silicates by this method and by the others employed suggests the necessity for further study. Possibly other silicates besides feldspar and talc will cause more reaction when sufficient quantities are thus concentrated in one small area. Time must demonstrate whether the initial change will progress to fibrosis. However, the practical significance of such massive doses remains doubtful.

ASBESTOS

The asbestos group of silicates, including anthophyllite, amosite, amphibole, crocidolite and chrysotile, have invariably failed to cause fibrosis or even early proliferation either intravenously in rabbits or in the peritoneal cavity of guinea pigs. Miller and Sayers [5] had a similar experience with three forms, chrysotile, amosite and crocidolite, and they classified them as inert substances. Obviously these observations are at variance with the well recognized capacity of asbestos to produce fibrosis of the lungs and demand explanation. One should not be too ready to condemn the method or to conclude that animals are incapable of reacting to asbestos. The method has worked consistently with free silica, and extensive pulmonary fibrosis has developed in guinea pigs when made to inhale chrysotile fibers. It is felt that the failure of these fibrous silicates to produce fibrosis in organs outside the lungs has real significance.

A very considerable number of observations are pointing to the hypothesis that the fibrous silicates behave in a different manner from the particulate minerals and that they irritate the lungs mechanically. Unlike quartz and the other active free silicas, not only have they failed to produce fibrosis in organs other than the lungs but they have not become more irritating as particle size decreases. Chrysotile fibers less than 3 microns in length are no more active than the silicate serpentine, which has the same chemical composition but is massive rather than fibrous in structure. Even by inhalation chrysotile, ground to such fineness that its fibrous structure is no longer recognizable, has produced no suggestion of fibrosis after a year's exposure. If its action were chemical, the reduction in particle size should have resulted in an accelerated tissue response. The fibrosis of asbestosis that occurs in the lungs is not characterized by the hyaline transformation characteristic of the chemical action of free silica. In experimental animals, at least, the fibrosis of pulmonary asbestosis does not progress after exposure to the dust is discontinued, as invariably happens with free silica. All these observations suggest a mechanical rather than a chemical form of irritation. It has been inferred that reaction to asbestos is restricted to the lungs because only these organs possess the proper structure and physiologic activity to permit friction with a stiff fibrous foreign body.

The most obvious objection to this hypothesis is concerned with the formation of that peculiar structure known as the asbestosis body. It is produced by a thick coating of iron and probably organic material laid down on the surface of an asbestos fiber. The deposit

TABLE 2.—*Combined Silica or Silicates*

		Rabbit's Vein		Guinea Pig's Peritoneum	
Group	Variety	Maximum Period Observed, Months	Tissue Reaction	Maximum Period Observed, Months	Tissue Reaction
Feldspar	Na-Microline	24	±	12	+
Pyroxene	Rhodonite	5	3+	4	+
Amphibole	Anthophyllite	12	+	12	+
	Amosite (fibrous)	6	±	4	+
	Na-Tremolite	12	±	12	±
	Amphibole	6	±	12	+
	Crocidolite	12	±	12	±
	Beryl	3¾	2+(d)	4	+
Garnet	Almandite?	24	±	12	±
Topaz	Sillimanite	24	±	12	±
Zeolite	Analcite	24	±	12	+
Mica	Muscovite	6	2+	4	2+
	Sericite (fibrous)	21	+	12	±
	Sericite (platy)	24	+(d)	12	±
	Biotite	4½	3+?(d)	8	+
Serpentine	Serpentine	12	±	12	±
	Chrysotile (asbestos)	9	+(d)	12	+
Talc	Talc	24	2+	12	2+
	Glauconite	12	+(d)	12	+
Kaolin	Dickite	6	2+	4	2+
	Halloysite	4	3+	4	2+
	Montmorillonite	3	2+	8	2+
Titano-silicates	Titanite	6	±	4	2+

d = sudden death.

9. Jones, W. R.: Silicotic Lungs: The Minerals They Contain, J. Hyg. **33**: 308-329 (Aug.) 1933.

is extremely irregular in outline with terminal globular swellings and numerous transverse haustrations. It is a golden yellow and, like the blood pigment hematoidin, it gives microchemical reactions to iron. In the lungs of guinea pigs, asbestos fibers must remain in contact with the tissues for about two months before the coating becomes recognizable. Asbestosis bodies also occur in man and have been reported in the lungs of brown rats.[10] In the lungs of cats, rabbits and white rats subjected to prolonged inhalation of asbestos dust they have never been discovered. In other organs they usually fail to develop; only in very rare instances have one or two bodies been detected in the peritoneal cavities of guinea pigs injected locally. They are reported as absent in the "asbestos corns" which appear on the hands of workmen handling this fibrous mineral.

The absence of asbestosis bodies in tissues other than the lungs suggests that chemical changes peculiar to that organ are responsible for their development. Since

TABLE 3.—*Nonsiliceous Minerals*

	Injections of						
	Rabbits		Guinea Pigs		Other Tests		
Mineral	Maximum Time Observed, Months	Tissue Reaction	Maximum Time Observed, Months	Tissue Reaction	Maximum Time Observed, Months	Tissue Reaction	Type of Test
Diamond	36	±	..	..	..	..	.....
Coal, bituminous	12	2+	12	+	41	±	Inhaled
Coal, anthracite (1.76% SiO_2)	12	±	12	±	12	0	Subcutaneous
Silicon	..	..	..	..	5	±	Subcutaneous
Aluminum oxide	24	±	12	±	12	±	Subcutaneous
Rutile	..	..	11	+	11	±	Subcutaneous
Marble	..	..	1	0	3	0	Subcutaneous
Gypsum, satin spar	12	2+?	..	..	..	..	.....
Gypsum, calcined*	..	..	5½	2+ (Calcif.)	24	±	Inhaled
Galena	..	..	12	Abscess and repair	..	..	.....
Chalcopyrite	..	..	12	±	..	..	.....
Iron sulfide	..	..	12	±	..	..	.....
Zinc sulfate (roasted sulfide ore)	11	2+	12	Abscess and repair	..	..	.....
Fluorite (0.8% SiO_2)	18	2+	11	2+	..	..	.....
Dolomite	1⅛	Death	0	Death	..	..	.....

* In the original publication [6] calcined gypsum was erroneously reported to have produced no reaction six months after injection into the ear veins of rabbits. This dust has not been tested by the intravenous method.

a fibrous reaction has been observed only in the tissues where the bodies have been numerous,[11] the question arises as to whether the chemical changes responsible for the deposit on the mineral fiber is the same one that affects the tissues of the host. No answer is yet available, but it is quite conceivable that the two effects are independent of each other. It has been suggested that the irritated tissues attempt to protect themselves by laying down the coating, and as a matter of observation subcutaneous injection of asbestosis bodies recovered by digesting human lung tissue with antiformin has caused no fibrosis in guinea pigs.

These observations would suggest that as a class the silicate minerals are not irritating because they contain silica, which is liberated by chemical action of body fluids. A few of them, like biotite mica, beryl and some of the kaolins, seem to have essential molecular structures capable of provoking acute inflammation or early proliferation. Their action has not been followed long enough to demonstrate whether these early reactions of the first three to six months will be followed by fibrosis. Other silicates of a fibrous structure may act as mechanical irritants in organs with appropriate architecture and functional activity.

SILICON CARBIDE

One compound of silicon, which is not a silicate but a carbide, deserves special mention because it has such widespread industrial use as an abrasive. It is known to commerce by various trade names such as "carborundum" and "crystolon." By any of the injection methods it has failed to cause even a suggestion of fibrosis. The particles are phagocytosed by cells which merely enlarge to accommodate the foreign bodies in their cytoplasm without the "epithelioid" alterations suggestive of slight toxicity. There has been no change in the original picture within a period of two years after the injection of the standard doses. In the scheme employed throughout this work the reaction to silicon carbide has been classified as ±. After inhalation for a period of two and one-half years the lungs show excessive focal accumulations of dust associated with slight degrees of chronic inflammation. The lack of fibrosis following the injection of particles of this exceedingly hard abrasive constitutes very good evidence for rejecting the properties of hardness and sharpness as a cause of such reaction.

NONSILICEOUS MINERALS

Similar tests have been performed with a number of pure minerals containing no silica. As indicated in table 3, none of them have caused primary fibrosis; a few have provoked slight chronic inflammatory reactions; some have been toxic. With large doses selected as standard, the "toxic" minerals have either caused immediate death (e. g., dolomite) or excited acute inflammations the healing of which resulted in scar formation. The response to massive doses of toxic substances, such as the sulfides, has no bearing on the subject of pneumoconiosis, in which the quantities inhaled could never approximate those used for injections.

Aside from the toxic reactions that healed with the formation of more or less scar tissue, none of these nonsiliceous dusts have produced any fibrosis. Diamond, the hardest known mineral, and aluminum oxide, a common abrasive in industry, are inert. Soft coal is slightly more irritating than anthracite. The reaction to the satin spar form of gypsum will in all probability prove to be quite inert when the tests are completed. It so happened that the last animal of the series to be killed showed somewhat more chronic inflammation than other members of the series, so that its effect is noted as "2 + ?" in the table.

MIXTURES OF FREE SILICA WITH OTHER MINERALS

Apparently there are certain substances capable of depressing the action of silica, and there may be others which accelerate it. As long ago as 1918 Haldane [12] expressed the belief that coal dust inhaled at the same time as silica prevented the development of silicosis. His belief was based on clinical statistics and on experiments performed by Mavrogordato.[13] By 1929 the latter seems to have lost faith in these observations, for he wrote "The presence of carbon in the air does not

10. Gloyne, S. R.: The Morbid Anatomy and Histology of Asbestosis, Tubercle **14**: 550-558 (Sept.) 1933.

11. The human cutaneous lesions may constitute an exception but there is some question as to the exact structure of these lesions.

12. Haldane, J. S.: Dust Inhalation in Mines: Effects on Health, Scientific Am. (Supp. 2225), Aug. 24, 1918, p. 119.

13. Mavrogordato, A.: The Etiology of Silicosis, Réunion de la Commission internationale permanente pour les maladies professionelles, Lyons, April 3-6, 1929.

appear to affect the changes produced by silica other than coloring them." Apparently most clinical observers also gave up the Haldane theory of a protective action by coal dust after several years.

Recently, however, experimental pathologists have renewed their interest in the idea. I have long been impressed by two observations; it is not at all difficult to produce nodular fibrosis by making small laboratory animals inhale relatively pure, free silica, but they do not react in a similar manner to mixed dusts in which the silica is associated with considerable amounts of other minerals. Prolonged inhalations of heavy concentrations of natural mixtures such as granite and ferruginous chert or of artificial mixtures composed of fine quartz and gypsum dust have not produced an effect commensurate with the quantity of silica available in the atmosphere. Rather than condemn the inadequacy of the experimental method, I have attempted to discover whether there are reasons for the apparent failures.

Injections indicate that the presence of various other minerals in a mixture may retard the usual reaction to silica, restricting the extent of tissue involvement and modifying the form of the cellular response. Different classes of minerals seem to be capable of acting in this manner. Some of them occur in natural combination with free silica; others have been added artificially. Not enough is known about inhibitors to evaluate their effects quantitatively or to attempt to classify them, but their action is sufficiently striking to deserve more than passing mention.

Table 4 summarizes the experience in a long series of experiments based on injection and on inhalation of mixtures of some form of active silica and other minerals. The table indicates that injection produces much more reaction than exposure by inhalation to a dust of the same composition. Even on injection, however, the response to a given quantity of silica is modified. Both the rate at which reaction develops and its intensity are affected. Quite naturally the modification is most marked in cases in which nonsiliceous elements are found in excess.

Table 4 indicates that a variety of minerals may inhibit the action of quartz in the body: iron oxide, coal and some constituent of granite, probably the silicates (feldspar or mica), but perhaps some other element present in smaller amounts. The series would suggest that inhibition is most effective in the presence of small amounts of silica. The experience with anthracite coal and crude fluorite which are contaminated with practically the same quantities of silica implies that not all inhibitors are equally potent. The reactions to the different doses of granite and chert are indicative of the relative importance of the two factors dosage and time. In the various tests on these two minerals, from three to ten times the quantity of silica necessary to produce marked progressive fibrosis has been injected, but in the presence of inhibitors cellular reaction has been delayed. In the case of granite, mature fibrosis has never appeared, and even after twenty-two months the cellular picture is the same as that produced by the quartz alone in one or two months. In chert the proportion of silica to iron oxide is higher, and hence it should not be concluded that iron is a less effective inhibitor.

The consistent results observed in all animals used to test this series of minerals containing increasing proportions of free silica makes it seem most probable that the principle of inhibition is a valid one. The mechanism by which inhibitors exert their effects has yet to be demonstrated. The bearing on the general problem of etiology is obvious, for one must conclude that the rate and severity of reaction do not depend solely on the amount of free silica in the mixture. They are inversely affected by the other components of the dust.

The dust from the South African gold mine contained 70 per cent of quartz and yet even in this proportion the silica is somewhat inhibited. Reaction developed slowly, and after sixteen months the silicotic lesions were less advanced than those of the pure quartz standard. Incidentally the sericite, which with platy muscovite and a trace of feldspar and possibly ilemite make up the remaining 30 per cent of this mixture, has failed to accelerate the action of the quartz as Jones hypothecated. Experimentally it has not itself caused fibrosis nor has it accentuated the effect of free silica.

There still remains for consideration the evidence which has been interpreted as indicative of accelerator

TABLE 4.—*Mixtures of Silica and Other Substances*

Mineral and Silica Content	Rabbits: Maximum Period Observed, Months	Rabbits: Tissue Reaction	Guinea Pigs: Maximum Period Observed, Months	Guinea Pigs: Tissue Reaction	Other Tests: Maximum Period Observed, Months	Other Tests: Tissue Reaction	Type of Test
Hematite (6% SiO_2).....	12	±	12	+	48+8*	+	Inhaled
Anthracite (10.13% SiO_2)....	12	±	12	+	21	0	Subcutaneous
Crude fluorite (10.39% SiO_2)	12 15½	3+ 4+	11	2+	11	±†	Inhaled
Granite (35% SiO_2)							
Usual dose=0.3 Gm. SiO_2..	12 15	2+ 3+	12	+	30	2+†	Inhaled
3 times usual dose=1 Gm. SiO_2	12 22	2+ 3+	..	..	..	..	.....
Ferruginous chert (50% SiO_2)							
Usual dose=0.5 Gm. SiO_2..	12 19	4+ 5+	12 12	3+ 3+	22½+26*	+	Inhaled
Twice usual dose 1 Gm. SiO_2	12	5+	..	..	..	..	.....
South African mine dust (70% SiO_2)	16	4+	12	3+	..	..	.....

*Forty-two months in the dusting room plus eight months in a normal atmosphere and similarly twenty-two and one-half months in the dusting room plus twenty-six months in a normal atmosphere.

† In one or two animals nodular fibrosis (4+) developed in the lymph nodes draining the lungs but pulmonary fibrosis was lacking.

substances. The matter came to light in the examination of a few persons engaged in the manufacture of soap powders who died after exposures of a few months or years. The first cases were reported by MacDonald, Piggot and Gilder [14] in England, and subsequently a few more were found by Chapman [15] and others in this country. It was shown that the soap powder contained large amounts of very fine silica and appreciable quantities of free alkali. On the basis of the solubility hypothesis it was postulated that unusual quantities of silica had dissolved in the alkaline medium and that a more rapid reaction had consequently developed. However, when some of these persons died and came to autopsy their lungs showed complicating tuberculosis.[16] A few sections from one of Chapman's patients reviewed by me revealed no evidence of complicating infection, but unfortunately such small blocks of tissue were available that one could not be certain that isolated foci of infection had been overlooked.

14. MacDonald, G.; Piggot, A. P., and Gilder, F. W.: Two Cases of Acute Silicosis (with a Suggested Theory of Causation), Lancet **2**: 846-848 (Oct. 18) 1930.
15. Chapman, E. M.: Acute Silicosis, J. A. M. A. **98**: 1439-1441 (April 23) 1932.
16. Kettle, E. H.: Personal communication to the author.

McCord, Fleming, Ainslee and Johnston [17] injected silica with alkalis into the peritoneal cavity of guinea pigs and found that the "primary toxicity" of silica was increased (one out of four of their animals injected with 0.4 Gm. of a mixture of equal parts of either quartz or silica gel and sodium bicarbonate died in four days). There was a wider dispersion of lesions than in the quartz control animals but there was "no proof of either accelerator or inhibitor action of alkalis in the production of silicotic nodules."

The similarity between the lesions found in the various "soap powder cases" and those in sand blasters and in certain tunnel workers [18] suggests the possibility that the rapidity and character of the cellular response might have been produced equally well by excessive concentrations of exceedingly fine particles. Definite proof of acceleration by alkalis is still lacking. It would be more logical to expect an immediate, acute, toxic reaction, the result which McCord and his associates obtained by injection.

Solubility of Silica.—Because so much has been written on the solubility of silica as the cause of its irritating properties, mention must be made of the attempts to evaluate this factor. It will be recalled that "the solubility hypothesis" was based on experimental proof of the toxicity of colloidal silica and the fact that quartz is slightly soluble in dilute alkalis. It was postulated that, since the reaction of the mammalian body is slightly alkaline, very fine particles of inhaled quartz might slowly dissolve and form the toxic colloid in the lungs.

Actual demonstration of solution of particulate silica in the living body is difficult both because the amounts are extremely small and because many tissues already contain small but variable quantities of silica which are apparently derived from ingested food. Gravimetric methods of analysis are inadequate to detect minute increases in quantity, and they do not differentiate between undissolved particles and silica in solution. In 1933 King and Stantial [19] modified Isaac's colorimetric method for determining soluble silica for use on biologic material so that it is now possible to detect minute quantities. To ascertain whether such silica is in true molecular solution or in the form of a colloidal suspension, the clear fluid is passed through an ultrafilter to remove the colloidal aggregates. According to King and McGeorge [20] the filtrate theoretically contains only silica in molecular solution.

By this method King, Stantial and Dolan [19] demonstrated an excess of silica in the urine of animals injected with soluble forms of this substance but lesser amounts when relatively insoluble quartz was substituted. They also reported that the urine of silicotic miners contained from four to five times as much silica as that of normal subjects. The latter observation was apparently confirmed by Sayers and Goldman [21] on a group of anthracite coal miners. Goldwater [22] then showed that the excretion of silica in normal human beings changes from day to day and that even on similar diets the urinary output varies in different workmen. Dworski [23] has confirmed Goldwater's observations and discovered that in addition to the leafy vegetables, which are generally recognized as the major source of ingested silica, certain brands of beer contain surprising amounts of this mineral. Drinking even a half a bottle of such beer will more than double the usual output of silica in the urine. On following the daily excretion in a group of nine tuberculous silicotic miners on ordinary diets for a period of months he found that in six of them the average output in twenty-four hours exceeded the daily average for a control group of normal subjects. However, only two had an average excretion greater than the maximum twenty-four hour output of the controls. In general it would appear that the daily fluctuation in urinary silica of normal persons is greater than the excess in the silicotic over the normal group. At the present time it is not generally conceded that the excretion of silica in the urine is of particular etiologic or diagnostic significance.

Theoretically it is debatable whether enough inhaled quartz can be dissolved, produce local tissue reactions and leave a surplus to be excreted in the urine. Comparatively small numbers of particles are inhaled into the pulmonary air spaces at any one time. They are phagocytosed and transported into localized areas where nodular fibrosis then develops. As evidence of local toxic action on the cells there are degenerative changes in the phagocytes and peculiar alterations in collagen. The former closely simulate the "epithelioid" degeneration produced by the tubercle bacillus; the latter consist of swelling, hyalinization and increased absorption of acid dyes. Although it has never been proved, it would seem very likely that most of the soluble silica would be fixed and retained in such reactions. Kraut [24] and later King and his associates [25] demonstrated little or no excess of silica in the blood of persons with silicosis. If it is carried in the blood to the kidneys for excretion it must exist in some other form than the toxic colloid, for anatomic evidence of damage to the kidneys or other organs is lacking. The statistical conclusions of Collis and Yule [26] that all the organs of the body are more frequently diseased in silicotic than in other subjects lack confirmation. To me it still seems probable that if the silica is dissolved most of it combines with the tissues in the immediate vicinity of the particles and that the soluble silica demonstrated in the urine is very largely derived from different foods. A carefully controlled study of the silica balance in hospitalized silicotic and normal subjects is indicated.

Recently many reports have appeared which deal with the solubility of silica outside the body. Some of them can be criticized on technical grounds. For example, Emmons and Wilcox [27] reported the solubilities of fine particles of quartz, flint and various silicates in blood serums. The particles were agitated in the serum at body temperature for periods of several

17. McCord, C. P.; Fleming, R. L.; Ainslee, Harriet, and Johnston, Jan: The Measurement of the Harmfulness of Dusts for Humans Through the Agency of Animal Reactions, Surg., Gynec. & Obst. **63**: 129-137 (Aug.) 1936.

18. Gardner, L. U.: The Pathology of So-Called Acute Silicosis, Am. J. Pub. Health **23**: 1240-1249 (Dec.) 1933.

19. King, E. J., and Stantial, Helen: The Biochemistry of Silicic Acid: I. Microdetermination of Silica, Biochem. J. **27**: 990-1001, 1933.

20. King, E. J., and McGeorge, Murray: The Biochemistry of Silicic Acid: V. The Solution of Silica and Silicate Dusts in Body Fluids, Biochem. J. **32**: 417-433 (Feb.) 1938.

21. Goldman, H. F.: Anthracosilicosis Among Hard Coal Miners, U. S. Pub. Health Bull. 221, 1936.

22. Goldwater, L. J.: The Urinary Excretion of Silica in Nonsilicotic Humans: Preliminary Report, J. Indust. Hyg. & Toxicol. **18**: 163-166 (March) 1936.

23. Dworski, M.: Unpublished data, Saranac Laboratory.

24. Kraut, Heinrich: Ueber den Kieselsäuregehalt des menschlichen Blutes und seine Veränderung durch Kieselsäurezufuhr, Ztschr. f. physiol. Chem. **194**:81, 1931.

25. King, E. J.; Stantial, Helen, and Dolan, Marjery: The Biochemistry of Silicic Acid: II. The Presence of Silica in Tissues, Biochem. J. **27**: 1002-1006, 1933.

26. Collis, E. L., and Yule, G. U.: The Mortality Experience of an Occupational Group Exposed to Silica Dust, Compared with That of the General Population and an Occupational Group Exposed to Dust Not Containing Silica, J. Indust. Hyg. **15**:395-417 (Nov.) 1933.

27. Emmons, R. C., and Wilcox, R.: A Mineralogical Study of Silicosis, Am. Mineralogist **22**:256-267, 1937.

weeks; portions of the suspension were then centrifuged at ordinary speeds (up to 3,500 revolutions per minute) to remove the particles, and the supernatant fluids were then analyzed gravimetrically for silica. Since it is doubtful whether all the particles less than 3 microns in diameter were removed from the viscid blood serum by centrifugation and since they determined silica by gravimetric analysis, which would detect both solid and dissolved material, their figures are probably too high.

Titus [28] attempted to overcome these difficulties by separating the particulate silica with an ultrafilter and by analyzing the filtrate colorimetrically, a method which should reveal only dissolved material. But King and McGeorge [20] point out that the dissolved material may exist in both colloidal and molecular solutions. As the colloidal ultrafilters remove not only particulate silica but also colloidal aggregates of dissolved silica, it is their opinion that Titus's very low solubility figures are also erroneous.

In the Saranac Laboratory the amount of soluble silica has been determined colorimetrically on all the physiologic salt solution suspensions of mineral particles used for testing animals. The particles in all cases are of a standard size; all are less than 3 microns in maximum diameter but in many instances those smaller than 1 micron have not been previously removed by elutriation. The suspensions are allowed to stand in a refrigerator until the supernatant fluid is water clear; a portion is decanted and centrifuged at high speed. Although one cannot be positive that every particle has been eliminated by this process, none can be seen; but even if particles were present they would not influence the result of the colorimetric analysis. The figures for free silica in these suspensions vary from values like 5.2 parts per million for active normal quartz to 205 for less active opal. In the case of the silicates the range is equally wide; the slightly irritating clay halloysite yielded 4.5 parts per million, while inert fibrous anthophyllite gave a figure of 124.2. The significance of these results remains to be demonstrated; the obvious deduction is that there is no parallel between the capacity of a siliceous mineral to produce reaction and its degree of solubility in physiologic solution of sodium chloride. Within wide limits the least soluble forms tend to be the most active tissue irritants, but even this is not always the case. For example, normal quartz and diatomite exhibit essentially the same capacity to form fibrosis and yet their corresponding solubility figures are 5.2 and 35 respectively. The moderately irritating opal yielded 205 parts per million of soluble silica, while inert silica gel gave 125 parts of soluble silica. Denny, Robson and Irwin [29] have shown that the solubilities of different samples of pure quartz vary widely, but no one has ever demonstrated a corresponding variation in the rate of capacity to provoke fibrosis. If these test tube experiments parallel conditions in the body, it would seem that some other factor besides solution in water is essential to the production of silicosis.

The last named authors and, shortly thereafter, Briscoe, Matthews, Holt and Sanderson [30] discovered that the addition of other minerals materially affected the solubility of quartz in water. For example, Denny and his associates reported that the addition of 1 per cent of fine metallic aluminum reduced the solubility of one sample of quartz from 50 to 1.9 parts per million. It was rendered more soluble by adding small quantities of the carbonates and hydroxides of magnesium, sodium, potassium and calcium. Briscoe and his co-workers likewise observed modified solubility of quartz but not always in the same manner and to the same degree; they reported that added magnesium carbonate, alumina and zinc oxide had no apparent effect on the yield of soluble silica from calcined flint, asbestos or feldspar.

These observations in vitro are most difficult to evaluate at the present time. The marked influence of other substances on solubility of silica suggests that such experiments may not be directly applicable to the living body. Attempts have been made to overcome the objection by substituting serum or ascitic fluid for water or salt solution as a solvent. King and McGeorge [20] report solubility figures for free and combined silica in these fluids which were comparable to those reported for water. Dworski [23] has obtained similar results in a few tests on normal quartz. King and McGeorge found, however, that the rate of solution was greater with several forms of free silica than with a few of the silicates. But even the use of a body fluid may not approximate conditions in the lungs, where change in hydrogen ion concentration may be more frequent and where the presence of appreciable quantities of other inhaled mineral particles may influence solubility.

Regardless of the mechanisms involved, all the experimental evidence tends to confirm the belief that fibrosis is to be expected only from various forms of free silica and from those silicates which have a fibrous structure; i. e., asbestos. The free silica need not necessarily be of crystalline form; one of the amorphous varieties has proved as active as normal quartz, although others were practically inert. A few of the silicates are toxic; others have produced mild degrees of cellular proliferation. If any of them ultimately cause fibrosis, such reaction must be extremely slow in development. Particles of certain other minerals naturally or artificially associated with free silica delay the development of silicotic fibrosis and modify its form. Whether all nonsiliceous minerals may act as inhibitors awaits demonstration. Definite proof of accelerators to the action of silica is yet lacking; it has been suggested that cases of "rapid silicosis" in human beings may be due to excessive exposures to silica or unusual fineness with or without associated infection.

Some information has been gained on the nature of the irritation produced by different minerals. It may be stated with reasonable certainty that the mechanical factors of hardness and sharpness play no part in the irritation from particulate minerals. With the fibrous silicates mechanical irritation is strongly suspected, although final proof is still lacking. The validity of the solubility hypothesis to explain the unusual activity of free silica has been questioned, and attention has been called to certain apparently well substantiated observations which are not consistent with the hypothesis as now conceived.

DUST INHALATION

Atmospheric Factors.—As already intimated, there are factors which exert a very marked influence on the behavior of dust suspended in air. If the dust is of

28. Titus, A. B.: Silica and Silicate Solubilities, J. Indust. Hyg. **19**:138-145 (March) 1937.
29. Denny, J. J.; Robson, W. D., and Irwin, D. A.: Prevention of Silicosis by Metallic Aluminum, Canad. M. A. J. **37**:1-11 (July) 1937.
30. Briscoe, H. V. A.; Holt, P. F.; Matthews, J. W., and Sanderson, P. M.: Some New Characteristic Properties of Certain Industrial Dusts, Institute of Mining and Metallurgy, London, 1937; Nature, London **139**:753 (May 1) 1937.

uniform composition the factors of specific gravity, particle size, capacity to absorb water and agglutinability largely determine how long it will remain in suspension. Obviously very heavy or very large particles will settle more quickly than smaller and lighter ones; those which remain separated longer than those which clump together and form heavy aggregates. The factor of particle size is of primary importance and has been the one most extensively studied. Sayers [31] has published a graph in which settling velocities are plotted against diameter for particles of various specific gravities. Most particles smaller than 1 micron in diameter settle at a rate of from 1 to 3 feet per hour. When the diameter exceeds 5 microns specific gravity has more influence; for a specific gravity of 7 the rate is 60 feet per hour, for 2.6, the specific gravity of quartz, it is only 25 feet per hour. With the exception of the fibrous materials, it may be said that any particle greater than 10 microns in diameter settles so rapidly that it plays a minor role in the formation of dust.

If the dust is produced from material of complex structure it should not be assumed, as is so often done, that the proportions of each constituent mineral will be the same either in the air or in the dust settled on the rafters as it was in the original rock. Variations in hardness and brittleness of different components will determine the size to which each will fracture. With a given expenditure of force a hard, tough mineral such as quartz will be broken into larger particles than softer materials. Because of their greater size the quartz particles may largely settle out of suspension, leaving an atmospheric dust composed chiefly of nonsiliceous matter. Numerous experimental and field studies made by the Saranac Laboratory have revealed convincing evidence of such variation in composition. A few examples are cited in the proceedings of the Third Symposium on Silicosis, held in 1937.[31a] Others are to be published in the near future. Hatch and Moke [32] found for example that in foundries the rafter dust might reveal 50 per cent or more of silica but that in air-floated material only 2.3 per cent of the particles under 10 microns in diameter were quartz. Subsequently Moke [32a] retracted his original conclusions because of errors attributed to his methods of analysis. Even then he was unable to ascertain the exact proportion of free silica in the atmosphere owing to the nature of the other components in the dust. In view of my own experience I am inclined to believe that the original conclusions of Hatch and Moke are still valid. Although many codes are still based on the silica content of the rock to be worked and numerous reports refer to analyses made on samples taken from rafters, it can be appreciated that such figures are not likely to be a reliable index of a dust hazard.

TABLE 5.—*Experiments on Inhalation*

		Silica Content			
Type of Rock	Particle Size	Ground Dust	Rafter Sample	Air-Floated Dust	Dust from Lungs, 1 to 2 Years' Exposure
Ferruginous chert A	50% > 3 microns Aver. 15 microns 50% < 3 microns Aver. 2 microns	51%	38%	10.5%	3.30%
Ferruginous chert B	90% < 2 microns	67.58	60.0	41.0	16.30
Mixture A Gypsum 1 part Quartz 1 part	All < 3 microns	49.70	53.7	28.3	.....
Mixture B Gypsum 2 parts Quartz 1 part	All < 3 microns	31.40	36.1	17.7	11.20
Quartz control	All < 3 microns	94.24	....	....	43.99

While differences in size, shape and specific gravity may influence the relative settling rates of individual particles in a mixed dust, the factor of agglutination also comes into play and probably has more significance than is the case of dusts composed of only one element. Particles of different physical or chemical structure often agglutinate to form masses so large that they cannot remain in suspension. Opposite electrostatic charges or hygroscopic properties are among the possible causes. If one of the elements happens to be free silica, agglutination with particles of some other mineral may materially reduce the percentage of silica remaining in the atmosphere. Examples of this effect will be cited later when the last group of factors has been discussed.

Factors of Protective Action of the Upper Respiratory Tract.—Whether the upper respiratory tract exerts any selective action on different kinds of mineral particles is unknown, but it would seem probable that dusts which are easily wet would be retained more readily than others. From an examination of the mineral particles which have gained access to the lung it is obvious that the protective mechanisms exclude practically all particulate material greater than 10 microns in diameter but that fibrous foreign bodies are not so effectively handled. Fibers of asbestos as long as 150 to 200 microns have been found in the alveoli. It would seem reasonable that aggregates of particles should be excluded in much the same manner as large single particles.

Probably because of the protective action of the upper respiratory tract, the composition of the mineral particles recovered from the lungs is often very different from that of the original rock and sometimes from the dust resulting from its manipulation. Examples from experiments on inhalation are illustrated in table 5.

The total concentrations of atmospheric dust as measured by the impinger method at the breathing level inside the animals' cages were excessive, for the four different experiments cited the average counts of particles less than 10 microns in diameter visible by light field illumination were as follows: chert A, 98,200,000; chert B, 551,800,000; gypsum-quartz mixture A, 319,000,000; gypsum-quartz mixture B, 303,000,000. By dark field illumination these figures were at least four times as high. In each of the chert experiments daily exposures of eight hours continued over a period of two years have failed to produce silicosis in rabbits, guinea pigs and white rats; only nonfibrous patches of chronic pneumonitis resulted. After three years, immature nodular foci of proliferation began to make their appearance.

During similar exposures to both of the artificial mixtures of quartz and gypsum, a few animals which were killed between the twentieth and the twenty-second month have revealed a limited number of atypical hya-

31. Sayers, R. R.: Third Symposium on Silicosis, Saranac Laboratory, 1937, p. 25, Employers Mutuals, Wausau, Wis.

31a. Durkan, T. M.: Third Symposium on Silicosis, Wausau, Wis., Employers Mutual Liability Insurance Company, 1937, pp. 67-69.

32. Hatch, Theodore, and Moke, C. B.: Composition of Air-Borne Foundry Dust, J. Indust. Hyg. & Toxicol. **18**: 91-97 (Feb.) 1936.

32a. Moke, C. B.: The Solubility of Quartz in Hydrofluosilic Acid, J. Indust. Hyg. & Toxicol. **18**: 299-300 (May) 1936.

line silicotic nodules in their lungs; those which survived longer had had no nodules but only the nonspecific pneumonitis.[33]

The explanation for the retarded development or the absence of silicotic reaction to the inhalation of these mixtures probably involves both the extrinsic and the intrinsic factors that have been discussed. In the case of the ferruginous chert, table 5 indicates that little silica had accumulated in the lung after exposure of one year. What did accumulate would be subject to the modifying action of the iron, previously demonstrated by injection. After three years of exposure enough silica had accumulated to cause reaction, but in the presence of the inhibitor the lesions were still immature and atypical. In the case of the gypsum-quartz mixtures the atmospheric factors were the only ones that have been evaluated. The table indicates low silica values for the lung ash in comparison with the quartz control series. After two and one-half years of exposure appreciable quantities of silica had begun to accumulate, but only in certain animals. Perhaps these were animals in which the protective action of the upper respiratory tract was deficient. The possible effect of intrinsic inhibitory factors has not been tested by injection of gypsum with quartz. In the case of granite dust the results of injection strongly suggest that the inhibition occurs inside the body, but here the extrinsic factors were not tested because facilities for chemical analysis were not available when the inhalation experiments were being made.

Similar inhibitory effects have been reported for metallic aluminum by Denny, Robson and Irwin.[29] These investigators found that the addition of only 1 part of aluminum to 100 parts of freshly fractured quartz prevented the development of silicosis in rabbits. In controls similarly exposed to pure quartz for sixteen hours a day perfectly typical early silicosis developed in six months. Their chemical analyses demonstrated as much silica in the lungs of the experimental animals as in the controls. In this case the inhibition unquestionably occurred inside the body.

Evidences of inhibitory action are not confined to experiments on animals; in industrial plants, reductions in the proportion of inhalable atmospheric silica have been repeatedly demonstrated and delayed responses to silica in mixed dusts are not uncommon. The studies of Hatch and Moke[32] on the reduction of the silica content in the atmosphere of foundries has already been mentioned. Similar observations have been made in unpublished surveys of cement and gypsum plants by Durkan.[34] In the former a quickly setting cement is made by adding a certain quantity of finely ground silica. In an intensive survey of conditions in seventeen such plants a theoretical dust hazard was anticipated from this process, but counts and analyses of the atmospheric dust showed low concentrations of silica at the breathing level. Physical and roentgenographic examinations of the workmen, more than 1,300 in number, have revealed only one person with silicosis attributable to mixtures of silica and cement dust. This man had had a severe crushing injury involving his face and nose which may well have been responsible. A damaged nose could easily impair the effectiveness of the upper respiratory protective mechanisms. In the gypsum industry, so-called "sanded plaster" was formerly made by mixing considerable quantities of fine and coarse sand with calcined gypsum. Here again the theoretical hazard was found not to exist after a study of the atmosphere and of the employees exposed. By special arrangement with their employers seventeen men, many of them retired, who had had long exposures in making this particular product were located and examined. Both physical and roentgenographic examinations failed to disclose a single case which was even suggestive of silicosis.

But on the other hand it may be objected that silicosis does develop in human beings who are exposed to mixtures of silica and other substances. As a matter of fact there are relatively few industrial atmospheres which are not mixtures, and silicosis does develop in many workmen when the silica content of the dust is sufficiently high. If so many fine silica particles are projected into the air that the other minerals fail to remove them they will be inhaled, but in many cases evidence of inhibitory action will still be manifested by a slow development of pulmonary disease. As examples, the very industries whose dusts have been the subject of experimental study may be cited: granite cutting and hematite mining. If one compares the average exposures that were necessary to produce demonstrable silicosis before the introduction of modern protective methods it will be found that they are much longer in these industries than in ones handling relatively pure silica. In the granite industry exposures of from fifteen to twenty years are commonly necessary to provoke nodular fibrosis; in the hematite mines the average is in excess of twenty years. With the purer silica dust of the lead and zinc mines of Picher, Okla., and the South African gold mines silicosis used to develop in from three to seven years.

In the past it has been customary to explain these variations in the rate of response in different industries on a basis of the relative quantities of free silica in the atmosphere. But the high total concentrations that are known to have existed before the campaign for the prevention of dust began to be effective have made this simple explanation seem inadequate. The action of the two sets of factors just described, one acting outside the body to reduce the amount of silica inhaled and the other inside the lungs to delay and modify the irritating effects of silica, may offer a more satisfactory explanation. Their effects are just beginning to be appreciated, and it will obviously require more study to determine their relative importance in any industrial atmosphere. At the present time it hardly seems justifiable to add protector substances to a siliceous dust as a prophylactic measure; at least, until more is known about the subject, the aim should be to decrease rather than increase the total amount of dust in the atmosphere.

FACTORS OF INDIVIDUAL SUSCEPTIBILITY

Up to this point the development of silicosis has been considered from the point of view of the group, and only average periods of exposure have been considered. It is a matter of common knowledge that not all members of any group react to inhaled dust in the same manner nor at the same rate. Every observer has been impressed with the fact that under the former conditions of employment only about one fourth of any group of miners of hard rock would develop silicosis while the other 75 per cent, apparently exposed in the

33. For reasons to be determined, the second gypsum-quartz mixture (2:1) was more active than the first, although the calculated quantities of silica at the breathing zone were almost the same in the two experiments.

34. Durkan, T. M.: Unpublished data from Saranac Laboratory.

same manner, seemed to be immune. Many explanations have been proposed but none are satisfactory. Some have believed that those who escaped were merely persons who did not happen to be exposed to enough dust for a sufficient period of time; some have held that the victims were mouth breathers or persons with deficient upper respiratory protective mechanisms, and still others have entertained the possibility of innate variations in the capacity of tissues to react to silica and other minerals. All investigators are agreed that coexistent pulmonary infection and particularly tuberculous infection plays a profound part in modifying individual susceptibility to inhaled dust.

It is obviously most difficult to prove whether any person in a large plant or even in a particular part of that plant has been subjected to the same quantity and quality of dust as his fellows. What has already been said of the variations discovered in a small experimental chamber 8 by 8 by 8 feet indicates the possibilitities in the large spaces of a mine or foundry. Dust counts and analyses may give some idea of average conditions if they are repeated sufficiently often, but no occupational history could possibly account for the rapid local fluctuation and summation of their effects.

Much has been written on effective nasal filtration in preventing or retarding the development of pneumoconiosis. Lehmann [35] has measured the efficiency of the nasal passages in miners and discovered that among men without silicosis 63 per cent had retention efficiencies for inhaled silica dust of over 40, and only 18 per cent fell below 30. In miners with silicosis only 20 per cent of the group had nasal efficiencies over 40, while 62 per cent were classified as less than 30. Lehmann like other observers feels that mouth breathers are in particular danger. These observations seem logical but they have not been confirmed, owing to the difficulty of making the measurements.

There is as yet no proof that the tissues of different normal persons vary in their capacity to react to irritating minerals. With the large doses of free silica employed for the injection tests every animal in any series has exhibited a similar response, and a capacity to react to silica has been proved for various mammals, birds, amphibians and fish. Possibly the injection of much smaller doses would demonstrate individual differences. A most desirable contribution would be a large series of chemical analyses of the lungs of both silicotic and nonsilicotic members of a human group exposed to some siliceous dust for a significant period of years. Intensive biochemical studies of both groups are also needed to answer this question.

The factor of infection is the cause for variation in susceptibility which has been studied most intensively. Relatively little is known of the effect of infections in the upper respiratory tract, although it is assumed that such conditions modify the protective mechanisms.

In the case of the lungs themselves there is no doubt of the etiologic significance of chronic infections. This complication may produce anatomic alterations which mechanically influence the deposition of inhaled dust, and it may possibly act in more subtle ways to alter the tissue responses to certain kinds of dust.

The mechanical effects are familiar and most easily understood. In normal lungs inhaled particles are probably distributed quite uniformly throughout the organs, except for a tendency to accumulation in the subpleural air spaces. By the agency of mobile phagocytes, ordinary quantities of such particles are removed from the air spaces and transported to the lymphatic vessels. Through the latter the foreign bodies are carried to lymphoid tissues situated both within and at the roots of the lungs. The development of a focus of chronic infection interferes with this orderly process of deposition and elimination. Appreciable numbers of air spaces may be obliterated by granulation or scar tissue, and the lymphatic drainage from the affected area is disturbed or perhaps destroyed. Particles of dust accumulate in increasing numbers about and within such an area of disease. The pigmented scars of healed tuberculosis in the apexes of the lungs are familiar examples of this tendency. The infectious process may be more extensive and may possibly have exhibited a considerable degree of pathologic activity during periods of inhalation of dust, but the same tendency to local accumulation is manifested. The subsequent development of emphysema and other changes to be discussed in the section on pathology may then make it appear that all the dust has localized in the region of the infection.

The more subtle influences of infection and particularly tuberculous infection in apparently altering the capacity of the lungs to react to siliceous dusts are not well understood. There are some investigators who believe that mature silicotic lesions never develop except in the presence of an element of infection. I do not subscribe to this view as I believe that the injection and inhalation experiments with pure silica have reproduced nodular fibrosis under conditions in which infection can be excluded. Nevertheless I admit that in some human lungs with even a localized focus of healed tuberculosis the nodules of silicotic fibrosis throughout all parts of the organs are of unusual size and appearance. I [36] have repeatedly maintained that the tubercle bacillus and silica dust in combination can produce results which neither irritant alone will do. With mixtures of free silica and other substances the inhibitors have not had their usual effects in animals infected with tubercle bacilli. The silicotic lesions have progressed more rapidly, and, while the tuberculous element has either healed or become very chronic, much more fibrosis has developed than with either infection or the dust alone. I have entertained the hypothesis that at least some of the silicates may prove to be more active on a background of infection than in normal lungs. Uncompleted experimental observations lend some support to this view, but the only silicate with which conclusive results have thus far been attained is chrysotile asbestos. Inhalation of this dust in association with any pulmonary infection has caused healing with much more fibrosis than either infection or asbestos alone. All these points will be more fully discussed in the section on pathology. Here it suffices to state that chronic infectious lesions and particularly those due to tuberculosis alter the localization and accumulation of all dusts in the lungs, that under proper circumstances they accentuate the development of silicotic fibrosis and that they permit both mixtures of free silica with other dusts and the silicate asbestos to produce unusual amounts of scar tissue.

7 Church Street.

35. Lehmann, Gunther: Dust Filtering Efficiency of the Human Nose and Its Significance in the Causation of Silicosis, J. Indust. Hyg. **17:** 37-40 (March) 1935.

36. Gardner, L. U.: The Relatively Early Lesions in Experimental Pneumoconiosis Produced by Granite Inhalation and Their Influence on Pulmonary Tuberculosis, Am. Rev. Tuberc. **4:**734-755 (Dec.) 1920.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS. HOWARD A. CARTER, Secretary.

NU-HESIVE SURGICAL DRESSINGS ACCEPTABLE

Manufacturer: Diadem Surgicals, Inc., Leominster, Mass.

New products utilizing Nu-Hesive Gauze Bandage as a base (acceptance published in THE JOURNAL, March 30, 1935, p. 1073) are recommended for use as sterile bandage or dressing material. Nu-Hesive is a nonabsorbent, porous material that traps excretions, adheres only to itself, and does not shrink when wet. Gauze is impregnated with a practically nonabsorbent cohesive latex which leaves the interstices of the fabric partially open. In addition to the Nu-Hesive Gauze Bandage previously accepted, the line includes Bias Bandage, Dia-Dressings, Finger Wraps, Gauze Tape Bandage and Ortho-Hesive Athletic Tape.

Nu-Hesive Bias Bandage: A bias bandage having considerable elasticity and binding pressure, in a range of sizes, used where excessive swelling is imminent or a slight flexing of the joint is desired.

Nu-Hesive Dia-Dressings: A prepared sterile compress, recommended in wet applications and as a dressing for boils, and ulcers. It is wrapped in individual glassine envelops.

Nu-Hesive Finger Wraps: A prepared, sterile finger dressing, for minor injuries, wrapped in glassine envelops.

Nu-Hesive Gauze Tape Bandage: A combination, nonshrinking tape and gauze bandage, packed in sterile rolls, especially useful in wet dressings.

Nu-Hesive Ortho-Hesive Athletic Tape: Primarily designed for ankle strapping for athletes; also useful in ankle and wrist support in serious sprain cases. Normal muscle flexing is permitted by a primary give or spring, and support becomes effective immediately following the limit of normal muscle action. The Ortho-Hesive Athletic Tape is not subjected to the same sterilization process since it is not intended to be used in contact with open wounds.

The firm was asked to substantiate the claims made for sterility and in reply submitted laboratory records, photographs of the testing laboratory in the finishing and packing rooms, and a test rack containing samples which had each been incubated for at least ninety-six hours at 37 C.

In addition, the materials were subjected to a bacteriologic examination by a competent medical man, at the Council's instigation. The report is abstracted here:

Materials and Methods.—Culture medium consisted of nutrient broth in large tubes (50 cc. in each tube) which was sterilized by 15 pounds steam pressure for twenty-five minutes. Instruments used in handling the gauze were wrapped in paper and sterilized by exposure to a temperature of 160-170 C. for at least two hours. All manipulations were carried out in a glass-walled box with an opening in the bottom on one side for the operator's arm. This opening was swabbed out thoroughly with saponated solution of cresol and kept closed for several hours before use.

The rolls of gauze were carefully unwrapped at one end and then securely grasped with a pair of heavy forceps by inserting one jaw through the hole in the center of the roll and the other jaw through the inner turns of the gauze. The wrapper was then entirely removed without allowing the outside of the wrapper to touch the gauze. By means of a safety razor blade held in a hemostat a number of deep cuts 0.5 cm. apart were made across the roll of gauze parallel to its axis. By means of a pair of forceps these sections were lifted out and placed immediately in the culture tubes. The inner spool, together with the few remaining turns of the gauze, was also cultured so that the entire roll of gauze was cultured each time.

The Finger Wraps and Dia-Dressings were opened by cutting off the end of the containing envelop. With sterile forceps the gauze was removed, rolled into a small roll and the entire piece placed in a culture tube. The tubes were incubated at 37 C.; half of the tubes of each series were incubated aerobically, the other half anaerobically in a sealed jar. It was shown that Clostridium sporogenes grew readily in broth tubes in the jar.

With each series of gauze culturing a number of broth tubes were opened and closed in the same manner as those receiving the gauze. These were incubated both aerobically and anaerobically.

Summary of Results.—One hundred and sixteen pieces of gauze, representing all the products submitted, were cultured in nutrient broth aerobically and anaerobically. No bacteria grew in any of the tubes. On inoculation of these tubes with Staphylococcus aureus and Bacillus subtilis growth occurred readily, with the exception of four series.

These were numbers 2, 9, 19 and 20, consisting of one-half inch Gauze Tape Bandage, 1½ inch Gauze Tape Bandage, 3 inch Bias Bandage and 4 Dia-Dressings (2 inches by 4 inches) respectively. Only slight growth in these showed that there is one inhibitory substance that is present in some of the preparations of gauze. This inhibition could not be correlated with any type of gauze or time of incubation. Since the inhibition was present in only a few of the rolls and then not in sufficient degree to prevent bacterial growth entirely, no attempt was made to remove the inhibitory substance. The tubes not showing this inhibition on inoculation showed as much growth as the control tubes.

It may be said that no bacteria were cultured from the products submitted, under conditions in which growth of ordinary bacteria occurred readily.

In view of the foregoing report, the Council on Physical Therapy voted to reaccept the Nu-Hesive Gauze Bandage and accept the Bias Bandage, Dia-Dressings, Finger Wraps, Gauze Tape Bandage and Ortho-Hesive Athletic Tape.

EMERSON HUMIDOX HUMIDIFIER ACCEPTABLE

Manufacturer: J. H. Emerson, 22 Cottage Park Avenue, Cambridge, Mass.

The Emerson Humidox is a humidifier for use in connection with an oxygen regulator and nasal catheter for administering oxygen to patients. It consists of a quart preserve jar with a metal cover equipped with an inlet which is attached to the regulator and an outlet which leads to the catheter. The inlet pipe goes to the bottom of the jar, which is partially filled with water. At the lower end of this pipe is a porous filter which breaks up the oxygen into very fine bubbles, allowing it to take up slightly more moisture than would be possible with an ordinary wash bottle, according to the firm.

Emerson Humidox.

The apparatus may be purchased with a carrying case and additional equipment including a regulator, catheter and wrench. When the Airco float type gage is used, corrections have to be made for the indicated flow. These are mentioned in the direction sheets.

With the large cover of the preserve jar held in place by a resilient fastener, any excess pressure causes this to act as a safety valve. Water does not pass through the walls of the porous filter rapidly, which aids in preventing sudden high pressures from escaping from the regulator into the jar and hence to the patient. In addition, it acts as a protection in case the humidifying jar is tipped over.

A separate heater may be hung on the humidifier. This raises the temperature of the water from 10 to 15 degrees, depending on the size of heating element used (from 10 to 30 watts). It is claimed that the warmed oxygen is better for the patient.

The only therapeutic claim made for the device by the manufacturer is that it will reduce the danger of drying out the nasal passages and the oropharyngeal mucosa when oxygen is being administered by nasal catheter.

In order to substantiate claims made for the unit, it was investigated clinically by a competent physician. He reported that it rendered satisfactory service.

In view of the foregoing report, the Council on Physical Therapy voted to accept the Emerson Humidox Humidifier for inclusion in its list of accepted devices.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, NOVEMBER 19, 1938

ANIMAL EXPERIMENTATION AND SCIENTIFIC MEDICINE ENDORSED BY VOTERS

The voters of California and Colorado, November 8, by overwhelming majorities emphatically rejected proposals made in those states to undermine the structure of scientific medicine. In California an initiative humane pound law, so called, proposing to cripple scientific research by hampering animal experimentation, was decisively defeated. In Colorado an initiative measure proposed by a group of chiropractors, to debase the quality of medical care in the state by repealing the basic science act and by destroying other safeguards that have been erected to assure adequate and scientific medical service, was met by an avalanche of negative votes, running as high as ten to one in some counties.

In Oklahoma an initiative measure that would have sanctioned practices not conducive to public welfare failed to get on the ballot, because of court action instituted by the medical profession. In Ohio a chiropractic initiative somewhat similar to the Colorado initiative died aborning, the cultist sponsors apparently becoming disheartened shortly after the proposal was submitted to the attorney general for his approval as to form. Petitions in Ohio were not circulated and the proposed initiative measure was not submitted to the people for a vote.

The medical associations in the states named assumed the lead in thwarting the selfish interests behind these proposals, interests that would subordinate the public welfare to their own private ends. In California and Colorado the state medical associations, aided by many lay and other professional groups and by public spirited citizens, informed the people fully of the dangers implicit in the proposals. To bring these dangers to the attention of the voters necessitated great sacrifices of time and money, but the results show that such sacrifices were well worth while and indicate that an informed electorate will support scientific medical care under proper legal and ethical safeguards.

INJURIES TO THE RECURRENT LARYNGEAL NERVE

The recurrent laryngeal nerve is a branch of the vagus nerve which on the right side arises in front of the subclavian artery and on the left side to the left of the arch of the aorta. On each side the nerve ascends in the groove between the trachea and the esophagus and enters the larynx, branches going to all the muscles except the cricothyreoideus. An injury to both recurrent nerves in the course of a thyroid operation is a calamity.

The prevailing attitude of surgeons toward the recurrent nerves, which is partly erroneous, has been unchanged from the beginning of thyroid surgery. Kocher's position in advocating that partial thyroidectomy be done under local anesthesia so that, in having the patient speak, the surgeon might learn that the recurrent nerves were not injured, was unsound. There are temporary changes in the voice in some patients immediately after and probably during thyroid operations without injury to the recurrent nerves, and, if the voice change does indicate an injury to the nerve, the damage has already been done. Other unsubstantiated impressions about the recurrent nerves have been accepted for many years. Surgeons have assumed that the nerves were too small to dissect and that, when possible, dissection would result in recurrent nerve paralysis. It has also been assumed that direct suture of severed recurrent nerves was impossible because the nerves could not be found in the scar tissue following subtotal thyroidectomy and if found they would be too small to suture. Recent experience at the Lahey Clinic [1] has shown that these assumptions are false. Three years ago Lahey undertook to demonstrate the recurrent nerve in practically all thyroid operations. To date the surgeons of that clinic have dissected more than 3,000 recurrent nerves, thus showing not only that the nerve is sufficiently large to be dissected but that it can be palpated as it is pushed laterally against the tracheal wall; also that routine dissection and even palpation while on a moderate stretch cause no interference with function. Moreover, this experience has proved that the routine exposure of recurrent nerves in thyroid surgery will diminish, if not largely eliminate, injuries to that nerve.

There is still some confusion about the clinical features of recurrent laryngeal nerve paralyses. If the recurrent nerves are interrupted there is usually little difficulty with the patient's breathing during the operation, but immediately after the operation the patient is unable to talk because of loss of innervation of the vocal cords. Frequently within six months the patient may report that the voice is returning. Somewhat later the patient will complain of inability to breathe satisfactorily after any unusual activity, and this condition will progress until there is difficulty with breathing on

1. Lahey, Frank H., and Hoover, Walter B.: Injuries to the Recurrent Laryngeal Nerve in Thyroid Operations; Their Management and Avoidance, Ann. Surg. **108**: 545 (Oct.) 1938.

slight exertion. Permanent bilateral abductor paralysis causes obstruction of the larynx by the mesial position of the vocal cords, relief from which often necessitates the permanent use of a tracheotomy tube.

After demonstrating the ease with which severed recurrent nerves can be approximated, Lahey states that, in all cases in which there is such an injury which does not disappear in three months, the nerve should be explored and the ends refreshed and anastomosed. The previous attitude generally has been that in such injuries nothing much could be done. In a case in which both nerves had been severed elsewhere ten months previously they were found and anastomosed without difficulty. One great difficulty of suturing recurrent nerves is that of approximating abductor fibers with abductor fibers and adductor fibers with adductor fibers. At present it is impossible to say whether restoration of double impulse nerve conduction in a single trunk can ever be successfully accomplished. One should, however, in anastomosing recurrent nerves make every effort to unite them so that there may be at least a reasonable chance of fibers conveying similar impulses being opposed to each other. With magnifying lenses it can be seen that the nerve is somewhat flattened. In uniting it the surgeon should place the two ends of the nerve in the same flat plane and with no twist in them. When more than half an inch to an inch is lost it is doubtful whether the severed ends of the nerve will come together.

Even though thyroid surgery is now well established on a sound basis, there is still need for more interest among surgeons in diminishing the incidence of injury to recurrent laryngeal nerves.

MIXED TUMORS OF THE LUNG

Discrepancies between the microscopic diagnosis and the clinical behavior of tumors are not infrequent. Cole [1] has recently cited many examples of gastric ulcer in which the estimation of malignancy varied decisively among various diagnosticians. A newer and more difficult problem concerns the diagnosis of tumors of the bronchi.

Formerly tumors of the lung were considered rare and quite unsusceptible of surgical attack, even when benign. Now, however, the point of view has changed. Not only are benign tumors considered suitable for successful surgical excision but even malignant neoplasms have been shown to be removable with comparative safety and with a reasonable chance of cure. With the emphasis on early diagnosis has come the identification of the early clinical manifestation of these tumors. The symptoms produced by pulmonary tumors are now becoming more generally known. With the advent of bronchoscopy their early stages are actually seen and biopsy specimens obtained and studied. Whereas our knowledge of neoplasms of the lung was formerly based on necropsy material, now bronchoscopic examinations with study of biopsy specimens are more frequent. With this advance has come an apparent increase in the incidence of such lesions but with it a confusion as to their actual nature. Especially important is the estimation of the malignancy of these early tumors. On such a diagnosis must rest the decision as to the most appropriate type of therapy. Many of them have been called adenomas, others have been described as polyps, a few as chondromas, fibromas, angiomas and neurofibromas.

When a patient complains of chronic cough, hemoptysis, pain in the chest or unexplained fever, the diagnosis of influenza or unresolved pneumonia may seem logical and correct. In many instances, however, a small tumor will be found occluding a bronchus, producing atelectasis or associated with pulmonary suppuration. With bronchoscopic relief of the obstruction the symptoms may disappear. However, microscopic study of the excised tissue may reveal a benign or a malignant lesion. Shall it be treated with diathermy, roentgen therapy or radium, or does surgical excision offer the only secure hope of cure? The answer to these questions is the subject of an anatomic and clinical study of many of these cases, recently reported in the Ludvig Hektoen festschrift by Womack and Graham.[2] These observers present evidence to show that many pulmonary neoplasms resemble fetal pulmonary tissue and arise from the failure of embryonic buds to develop into normal structures. Recognizing their similarity of behavior and in some respects their similarity of origin to the mixed tumors of the parotid gland, these workers have described this group of neoplasms as mixed tumors of the lung and have built up a histologic and clinical entity to fit their observations.

This new concept of pulmonary neoplasms will probably go far to explain the discrepancies which have been experienced in the microscopic appearance and clinical behavior of many tumors of the lung. As Womack and Graham point out, these tumors arise from entoderm and mesoderm and hence may take various forms depending on the tissue they resemble. More important is the fact that these tumors, though at first benign, may eventually develop into carcinoma and are to be considered, therefore, as potentially malignant. By the time they do become malignant their pathogenesis is lost and they may look like the ordinary type of bronchiogenic carcinoma. Thus is explained the failure of postmortem studies to recognize this group of tumors. With the realization of their common origin as mixed tumors, Womack and Graham feel on the basis of their studies that such terms as adenocarcinoma, alveolar carcinoma, mucous gland carcinoma, "oat cell" carcinoma and round cell carcinoma are now untenable. With this simplification in the terminology as well as

1. Cole, L. G.: The Pathological Yardstick: Its Accuracy as an Instrument for Measuring Errors in Clinical, Roentgenological and Surgical Diagnosis of Gastric Lesions, Surg., Gynec. & Obst. **63**: 689 (Dec.) 1936.

2. Womack, N. A., and Graham, E. A.: Mixed Tumors of the Lung: So-called Bronchial or Pulmonary Adenoma, Arch. Path. **26**: 165 (July) 1938.

pathogenesis, the study of the early manifestations of pulmonary neoplasms will be facilitated. Perhaps the growing incidence of the late stage of inoperable cancer of the lung may be halted by a recognition of the lesion which in many cases seems to be its precursor.

Current Comment

BUILD OF WOMEN AND MORTALITY

In a preliminary report read before the Association of Life Insurance Medical Directors of America, Dublin and Marks [1] discussed the results of their investigations on the relation of height and weight of women to the death rate. Their descriptive tables are based on 329,627 policies and their mortality tables on 308,228 policies—material extensive enough for statistical conclusions in most classes even though derived from the experience of a single company. When all heights were combined, the most favorable mortality in ages under 30 was found among those slightly (from 5 to 14 per cent) and moderately (from 15 to 24 per cent) overweight; but the ratios for these groups were not significantly different from those of average weight. From these low levels the mortality increased to its highest point in the 25 to 35 per cent overweight, followed closely by those from 15 to 24 per cent underweight. At ages 30 to 39 the situation was in many respects similar. At ages 40 to 49 the best mortality was recorded among those slightly below average weight, and at ages 50 and over the most advantageous mortality was among those who were underweight. In the aggregate the mortality of women of short height has been distinctly above the average, and the ratio of actual to expected deaths was 109 per cent for this group as compared with 98.8 per cent recorded for both medium height and tall women. This excess mortality of short height women appeared in every age group. At ages under 30 the most favorable mortality was recorded among medium height women, but between 30 and 39 tall women have done best. In women over 40 there was in the aggregate no marked difference between the mortality ratio and the medium height and tall women. When related to specific diseases, mortality from tuberculosis was 60 per cent higher among those 15 per cent or more underweight than the average for the group. In those 15 per cent or more overweight the mortality was only 33 per cent of the expected. The mortality from pneumonia and influenza followed a similar pattern. Deaths from lobar pneumonia were highest among the underweight and those considerably overweight, although this trend showed much variation with age. For the chronic cardiovascular and renal conditions there was a fairly steady progression of the ratios from the lowest levels in the underweight groups to the highest in the overweight groups. Acute heart and kidney disease, on the other hand, tended toward high frequency among the underweight. Diabetes showed the typical correlation between weight and mortality far more distinctly than did most other causes. The most striking differences in mortality were found in diseases of the gallbladder and biliary passages, where there was an unmistakable progression of mortality from a low point among the underweight to a high point among those who were more extremely overweight. This study, while of a preliminary nature, apparently serves to confirm the general assumption that has been made in the insurance business with regard to the build of women; namely, that they present a situation similar to that disclosed by the studies of the influence of build on mortality among men. Furthermore, these authors believe, the anthropometric data indicate the need of some revision of the standard height-weight table, which is too smooth and therefore probably disregards fundamental changes in weight according to age during adult life. It is their opinion that median weights are probably better than mean weights because the latter are unduly influenced by extreme overweight.

1. Dublin, L. I., and Marks, H. H.: The Build of Women and Its Relation to Their Mortality, read at the forty-eighth annual meeting of Association of Life Insurance Medical Directors of America, Oct. 29, 1937.

TRANSPLANTATION OF HUMAN CANCER INTO RABBITS

Recently successful transplantation of human cancer into the anterior chamber of the rabbit eye has been reported. This is potentially an exceedingly important contribution to experimental pathologic technic. About a year ago Greene and Saxon [1] of the Rockefeller Institute, Princeton, N. J., tested the autoplastic and homoplastic transplantability of rabbit uterine adenomas and adenocarcinomas. While autotransplantations were invariably successful, intratesticular, subcutaneous, intramuscular and intraperitoneal transplantations into a new host invariably failed. Transplantations into the anterior chamber of the eye of a new host, however, were successful in a large percentage of the cases. After growth for from three to five serial transplants in the anterior chamber of the eye, successful transplants could be made into the testicle. With this encouraging result, the Rockefeller Institute experimenters retested the possibility of heteroplastic transplantation. Heteroplastic transfer of mammalian tissues is generally considered impossible. Two tumors, an adenocarcinoma of the rabbit uterus and an adenocarcinoma of the rabbit breast, however, were successfully transplanted into the guinea pig eye. Serial transplants through three generations were effected, a process which apparently could be continued indefinitely. In his latest report Greene [2] tells of attempts at similar heteroplastic transplantation of a human breast tumor. Seven successful takes were obtained in twelve attempted transplantations into the anterior chamber of the rabbit eye. Growth first became apparent toward the end of the third week, with vascularization readily visible during the sixth week. Following vascularization the growth rate increased. Since the behavior of the human cancer grafts in the rabbit eye conforms in all respects to those of rabbit tumors in the guinea pig eye, Greene believes that human tissues can thus be maintained and cultivated indefinitely in the rabbit. If so, his technic may be applicable to a wide range of physiologic and pathologic problems not associated with malignant growths.

1. Greene, H. S. N., and Saxon, J. A., Jr.: J. Exper. Med. **67**: 691 (May) 1938.
2. Greene, H. S. N.: Science **88**: 357 (Oct. 14) 1938.

ORGANIZATION SECTION

HOUSE OF DELEGATES COMMITTEE MEETS WITH INTERDEPARTMENTAL COMMITTEE

On October 30 the Committee of the House of Delegates of the American Medical Association, including Dr. Irvin Abell, President of the Association, as chairman; Dr. Walter F. Donaldson, Pittsburgh; Dr. Walter E. Vest, Huntington, W. Va.; Dr. Henry A. Luce, Detroit; Dr. Fred W. Rankin, Lexington, Ky.; Dr. Frederic E. Sondern, New York; Dr. E. H. Cary of Dallas, Texas, with Dr. Rock Sleyster, President-Elect of the American Medical Association, and Dr. Olin West, Secretary, ex officio, met with the Interdepartmental Committee to Coordinate Health and Welfare Activities of the Government in Washington. The Interdepartmental Committee arranged for attendance by several members of its own Technical Committee, and the American Medical Association group was accompanied by Dr. W. C. Woodward of the Bureau of Legal Medicine and Medical Legislation and Dr. R. G. Leland and Mr. Jack D. Laux of the Bureau of Medical Economics.

In a joint interview, following the conference, by Dr. Irvin Abell and Miss Josephine Roche, it was pointed out that the conference had reached no definite conclusions or specific plans for cooperation, nor had there been any abandonment of specific positions taken by either group in relationship to the program. The representatives of the government again explained the detailed concept of the National Health Program. The representatives of the American Medical Association indicated the actions taken by the House of Delegates, which involved approval of the extension of public health service specifically related to the prevention of disease and the provision of hospitals and allied institutions and of government assistance for the care of the indigent when the need can be established. The medical representatives pointed out that in hospitalization and the care of the indigent the administration should be simple and placed in the hands of responsible public officials who would cooperate with local medical societies. The medical representatives again expressed opposition to compulsory sickness insurance and the fear of the fact that the insistence on such a system by the government would be "bureaucratic, costly and political."

In a brief report on the conference, President Irvin Abell said:

> The reception accorded our committee was quite friendly and the discussions evinced the same spirit on both sides. They were fruitful in bringing out a better understanding of opposing points of view and in focusing attention on the discrepancies in data and statistics on which such points of view are founded. While tentative agreement in principle, not in methods of application, was reached on four of the recommendations, the conference was stymied by the question of compulsory sickness insurance. The Interdepartmental Committee is to hold conferences with representatives of other groups, notably the American Public Health Association, the American Dental Association, the American Hospital Association and the American Nursing Association. It was suggested that our committee return at a later date for further conference presumably after the above named organizations, through their representatives, have had opportunity to express their views. If this invitation is accepted an early date was suggested, as the Interdepartmental Committee will prepare its report to be submitted to the President at the opening of the Congress, when its recommendations may be embodied in proposed legislation.

ABSTRACT OF REPORT OF SPECIAL COMMITTEE OF THE AMERICAN DENTAL ASSOCIATION

Your committee [of the House of Delegates of the American Dental Association] has drawn up the following declaration of principles and recommendations which it believes should be presented by the American Dental Association to the federal government for its assistance in planning the dental phase of a general health program.

Your committee recommends that in the formulation of any national health program the American Dental Association should insist on including the following principles:

I. In all conferences that may lead to the formation of a plan relative to a national health program, there must be participation by authorized representatives of the American Dental Association.

II. The plan should give careful consideration to: first, the needs of the people; second, the obligation to the taxpayers; third, the service to be rendered; and, fourth, the interests of the profession.

III. The plan should be flexible so as to be adaptable to local conditions.

IV. There must be complete exclusion of nonprofessional, profit-seeking agencies.

V. The dental phase of a national health program should be approached on a basis of prevention of dental diseases.

VI. The plan should provide for an extensive program of dental health education for the control of dental diseases.

VII. The plan should include provision for rendering the highest quality of dental service to those of the population whose economic status, in the opinion of their local authorities, will not permit them to provide such service for themselves, to the extent of antepartum care, the detection and correction of dental defects in children, and such other service as is necessary to health and the rehabilitation of both children and adults.

VIII. For the protection of the public, the plan shall provide that the dental profession shall assume responsibility for determining the quality and method of any service to be rendered.

RECOMMENDATIONS

Your committee has considered the five recommendations of the Technical Committee and, so far as they apply to dental service, makes recommendations as follows:

Expansion of Public Health and Maternal and Child Health Services.—Expansion of General Public Health Services: 1. We approve of the general expansion of public health services and, in addition, recommend the establishment of a federal Department of Health with a secretary who shall be a graduate in medicine, and a member of the President's cabinet; and a first assistant secretary who shall be a graduate in dentistry.

2. In an expanded public health program which involves a consideration of the expenditure of millions of dollars for public health purposes, your committee recommends that the problem of dental caries and other dental diseases be included.

Medical Care for the Medically Needy and a General Program of Medical Care.—1. Your committee is convinced that satisfactory dental service cannot be rendered under a compulsory health insurance system. We therefore do not favor such a plan but do approve voluntary budget plans under professional control which will enable patients to "apportion costs and timing of payments so as to reduce the burdens of [dental] costs and remove the economic barriers which now militate against the receipt of adequate [dental] care." [1] [The word "dental" was substituted by the committee for the word "medical" in the original quotation.]

2. The committee approves the recommendation that such a program should provide for "continuing and increased incentives to the development and maintenance of high standards of professional preparation and professional service." [1]

CONCLUSION

Your committee agrees with the Technical Committee's belief "that, as progress is made toward the control of various diseases and conditions, as facilities and services commensurate with the high standards of American medical practice are made more generally available, the coming decade, under a national health program, will see a major reduction in needless loss of life and suffering—an increasing prospect of longer years of productive, self-supporting life in our population." [2] We also believe that the above statements apply equally to dental practice and that the enumerated benefits would be enhanced by early and regular dental care in childhood.

Your committee offers two final recommendations:

1. In view of the fact that dental caries is the most prevalent disease of mankind, the American Dental Association strongly recommends that the federal government augment, with a comprehensive research program, the efforts of the organized dental profession to determine the cause of this disease.

2. That in keeping with the first main principle of this report, a committee of five practicing dentists be appointed by the Board of Trustees, together with such technical advisers as the needs of the committee require, to fulfil the provisions of principle I.

COMMITTEE

HOMER ROBISON. W. O. TALBOT.
CRAFT A. HOPPER. ALFRED WALKER.
E. E. VOYLES. STANLEY RICE.
HENRY CLINE FIXOTT. R. J. RINEHART.
HAROLD W. OPPICE, Chairman.

1. "A National Health Program," recommendation 4, paragraph 4.

2. "A National Health Program," recommendation 5, last paragraph.

OFFICIAL NOTES

HEARINGS BEFORE THE GRAND JURY IN WASHINGTON

In addition to witnesses mentioned in recent issues of THE JOURNAL, the newspapers report the following persons as having appeared last week before the Special Grand Jury in Washington, D. C.: Dr. Lewis H. Taylor, president of the Sibley Hospital; Mr. and Mrs. Charles Hardin; Mr. Sherwood Booth; Miss Tommie Lee Nix and Miss Elizabeth Tew, employees of the Home Owners' Loan Corporation; Miss Taylor Owen (the last three were said to be members of the Group Hospital Association, Inc.); Mrs. Peggy O'Connor and Mr. James R. Adams, both employees of the WPA; Miss Sarah Abbott, Mrs. Harriet A. Austin, Mr. and Mrs. H. P. Avery, all said to be members of the Group Health Association, Inc., and Dr. William W. Bauer, director, Bureau of Health Education, American Medical Association. The Grand Jury is also said to have had before it during the last week records of Garfield Memorial Hospital, brought by Dr. Francis J. Eisenman, superintendent, and records of Columbia Hospital for Women and Lying-In Asylum, brought by Col. P. M. Ashburn, superintendent of that hospital.

RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company, entitled "Your Health," began Wednesday October 19 and will run consecutively for thirty-six weeks. The program is broadcast over the Blue network of the National Broadcasting Company each Wednesday at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).[1]

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The next six programs to be broadcast, together with their dates and their topics, are as follows:

November 23.	Weather and Wearing Apparel.
November 30.	Rest, Relaxation and Recreation.
December 7.	Tuberculosis and the Teens.
December 14.	What Shall We Eat?
December 21.	Hidden Treasures in Foods.
December 28.	Good Milk, Good for You.

1. Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over Station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.

WOMAN'S AUXILIARY

California

The Santa Barbara County auxiliary recently gave $34 to the troup of Girl Scouts it sponsors in order that two girls might attend camp two weeks each.——At a benefit dinner at the residence of Dr. and Mrs. William Daniel, Pasadena, $370.66 was realized with which a resuscitator for babies was purchased and presented to St. Luke's Hospital, Pasadena.——The Santa Clara County auxiliary is holding a series of 50 cent teas in private homes, the profit from which is turned over to the charitable fund, with which a number of children each year are sent to camps.

Washington

Mrs. J. B. Robertson of the auxiliary to Pierce County Medical Society, Tacoma, won the special cash prize of $25 offered by the "Hygeia" Committee of the Woman's Auxiliary to the American Medical Association for the best paper on "The Value of 'Hygeia' to the Medical Profession." Only the auxiliaries winning cash prizes or honorable mention in the second *Hygeia* annual contest were eligible to participate.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Proposed "Humane Pound" Law Defeated. — The so-called humane pound initiative measure was defeated in the California election November 8 by a margin of more than two to one, according to press reports. Up to November 10 the totals were 1,259,014 votes against the measure and 593,934 in its favor.

Changes in Health Officers.—Dr. Alexander B. Bigler has been appointed city health officer of Chowchilla, succeeding Dr. Alton C. Atwood. Dr. Cornwall C. Everman is health officer of Larkspur and Dr. David G. Smith of Corte Madera; both of these communities were formerly served by Dr. Louis L. Robinson. The city of Needles has transferred the administration of its public health affairs to the San Bernardino County full time health unit; Dr. Walter W. Fenton is the health officer of the county. Dr. Frederick W. Knight has been appointed health officer of Corcoran to succeed the late Dr. James H. Van Vorhis.

CONNECTICUT

Society News.—Dr. Morton Arnold, Willimantic, addressed the Tolland County Medical Association October 18 in Somers on "Treatment of Common Diseases of the Ear, Nose and Throat."——The Hartford County Medical Society was addressed October 25 in Bristol by Dr. Abraham Myerson, Boston, on "Relationship of the Autonomic Nervous System to Pharmacology."——Dr. John A. Hartwell, New York, discussed "Trends in Medical Practice" before the New Haven County Medical Association October 27.——Dr. Rudolf Schoenheimer, New York, discussed "Studies in Protein Metabolism with the Aid of Heavy Nitrogen" before the Yale Medical Society November 9 in New Haven.

Changes in Health Officers.—Dr. Robert E. Perdue was appointed the first full time health officer of Norwalk, effective September 1. Norwalk is now the ninth city in Connecticut to be on a full time basis. Dr. William Sherman Randall has been appointed health officer of Shelton to fill the unexpired term of the late Dr. John E. Black. Dr. Donald J. McCrann, West Hartford, has succeeded Dr. Maurice B. Thompson as health officer of Bloomfield. Dr. Archibald M. Gaulocher, Wingdale, N. Y., is health officer of Kent and Dr. Frank D. Ursone, Norfolk, health officer of Colebrook. Dr. Edward J. Brophy is health officer of Norwich, filling the unexpired term of the late Dr. Harrison Gray.

DELAWARE

State Medical Election.—Dr. Meredith I. Samuel, Wilmington, was elected president of the Medical Society of Delaware at its annual meeting in Dover October 12. Other newly elected officers are Drs. Bruce Barnes, Seaford, and Charles G. Harmonson, Smyrna, vice presidents; John H. Mullin, Wilmington, secretary, and Alfred L. Heck, Wilmington, treasurer.

ILLINOIS

New District Health Units.—A new district health department has been established in Woodstock to serve the counties of Boone, Lake, McHenry and Winnebago. Dr. John F. Shronts is the district health officer.——Dr. Maurice Gore, Aurora, has been appointed medical officer in charge of the new health district embracing the counties of DeKalb, Grundy, Kane, Kendall and LaSalle. A new unit including Bond, Clinton, Madison and St. Clair counties has been placed under the direction of Dr. Claude Milton Eberhart, Highland.

Chicago

Personal.—Dr. Paul C. Barton, since 1934 a member of the staff of the Council on Pharmacy and Chemistry, has been appointed Director of the Bureau of Investigation of the American Medical Association. Following graduation from the University of Maryland School of Medicine, Baltimore, and completion of his internship, Dr. Barton spent several years in private practice.——Mrs. Lucille Smith, director of medical service for the Chicago Relief Administration, resigned October 6 to accept a position with the Social Security Board in Washington, D. C., newspapers reported.

Symposium on Blood Transfusions.—The Chicago Medical Society devoted its meeting November 9 to a symposium on blood transfusions. The following spoke:

Dr. Bernard Fantus, The Blood Bank of Cook County Hospital (Preserved Blood versus Fresh Blood).
Dr. Elizabeth H. Schirmer, Blood Preservation Technic.
Dr. Karl A. Meyer, Blood Transfusion Technic.
Dr. Lindon Seed, Blood Transfusion Reaction.
Dr. Egbert H. Fell, Transfusion of Fresh Blood.
Dr. Josiah J. Moore, Practical Possibilities of Private Blood Banks.

IOWA

Symposium on Fractures.—A symposium on fractures was presented before the Pottawattamie County Medical Society in Council Bluffs November 7 by the following:

Dr. Robert D. Schrock, Omaha, Fractures of the Ulna and Radius at the Wrist.
Dr. Hiram Winnett Orr, Lincoln, Neb., Prevention and Control of Infection in Fractures and Other Bone Surgery.
Dr. Arthur Steindler, Iowa City, Fracture Deformities of the Ankle.
Dr. Karl R. Werndorff, Council Bluffs, Fractures of the Spine.
Dr. Charles L. Scudder, Boston, Regional Fracture Committees of the United States and Fractures of the Os Calcis.

Refresher Courses. — Two refresher courses in obstetrics and pediatrics opened early in October in the eleventh and ninth councilor districts, under the auspices of the speakers' bureau of the state medical society, the State University of Iowa College of Medicine, Iowa City, the Iowa Pediatric Club, the Central Association of Obstetricians and Gynecologists and the state department of health. In the eleventh district the first two meetings were held in Atlantic, the next three in Red Oak, and the last three will be given in Harlan. The entire program for the ninth district is being presented in Chariton. The speakers include Drs. Everett D. Plass, John H. Randall, William F. Mengert, Philip C. Jeans, Julian D. Boyd, all of Iowa City; Robert M. Collins and Jack V. Treynor, Council Bluffs; Robert H. McBride, Sioux City, and Fred Moore, Des Moines.

LOUISIANA

Society News.—At a meeting of the Orleans Parish Medical Society in New Orleans October 24 the speakers were Drs. Lucien A. LeDoux on influence and effects of toxemias on menstruation; Leon J. Menville, "Treatment of Advanced Carcinoma of the Cervix," and Robert H. Bayley and David E. Fader, "Congenital Cystic Lung Disease."——Dr. Harold R. Cummings, Los Angeles, gave a talk on Metchnikoff before the Tulane History of Medicine Society, New Orleans, October 21.

Drive Against Illegal Practitioners.—J. E. Garret was fined $100 for practicing medicine without a license and $1,000 for selling improperly labeled products in court at Abbeville recently; $700 of the larger fine was suspended. Newspapers reported this as the first major conviction obtained by the state board of health in its drive against the illegal practice of medicine and the misbranding of preparations. It was also stated that forty manufacturers who had not registered with the board applied for certification of their products after recent seizure of eighteen uncertified products.

MARYLAND

Dr. Williams Reappointed Commissioner of Health.—Dr. Huntington Williams has been reappointed commissioner of health of Baltimore for another term of six years. Dr. Williams first became commissioner Jan. 31, 1933, after having served as director of health from Oct. 1, 1931.

Parrots Forbidden in Baltimore.—The mayor and city council of Baltimore approved an ordinance October 3 prohibiting bringing into, offering for sale, selling, giving away or breeding within the limits of Baltimore parrots, parrakeets, love birds, macaws, cockatoos, lories, lorikeets and other birds of the psittacine family. The ordinance provides that zoologic gardens operated under public authority or laboratories in which scientific research is being carried out may receive or import birds of the psittacine family in conformity with such rules and regulations as prescribed by the city department of health.

Society News. — The Baltimore City Medical Society met with the Medical Society of the District of Columbia November 16 in Washington; the speakers were Drs. Edmund L. Keeney on "Slow Epinephrine"; Hugh H. Young, "Genital Abnormalities of Hermaphroditism and Related Adrenal Diseases," and Monte Edwards, "Rectal Lymphogranuloma."

Dr. William Barry Wood Jr. addressed the Baltimore society November 4 on "Treatment of Lobar Pneumonia." A symposium on vitamins was presented before the Baltimore society October 21 by Drs. Julius Friedenwald on "Gastrointestinal Aspects"; Paul W. Clough, "Neurologic Aspects," and Esther L. Richards, "Psychiatric Aspects."

MICHIGAN

Society News.—Dr. James A. Conner, Chicago, addressed the medical section of the Wayne County Medical Society, Detroit, October 10, on "Treatment of Pertussis." The surgical section was addressed October 24 by Dr. Hans Finsterer, Vienna, Austria, on "Surgical Treatment of Acute Gallbladder Diseases and the Common Duct Obstructions."——Dr. Sabina Kessler-Frux, Bay City, was elected president of the Michigan branch of the American Medical Women's Association at the annual meeting in Detroit in September, succeeding Dr. Mary Margaret Frazer, Detroit.

Course in Basic Ophthalmology.—A new course in basic ophthalmology began November 1 at Wayne University College of Medicine, Detroit, to continue each Tuesday and Friday throughout the year. Designed for residents and those interested in increasing their basic knowledge in ophthalmology, the first course is on histology, comparative and human, while the second will be in physiologic optics, physiology of the eye, gross anatomic sections of the head and neck and so on. There is no fee for the courses. Dr. Parker Heath is professor and head of the department of ophthalmology.

Changes in Health Officers.—Dr. Philip E. M. Bourland, Lansing, recently associated with the state board of health, has been appointed director of the Dickinson County health unit, succeeding Dr. Clifton E. Merritt, Bay City, who accepted a similar position in Bay County. Dr. Russell E. Pleune, Lansing, who was scheduled to take over the post in Dickinson County, is now director of the Houghton-Keweenaw health unit, succeeding Dr. Forrest J. Austin, Houghton. Dr. Guy R. Post, Fremont, has resigned as director of the Tri-County Health Unit, serving Newaygo, Lake and Oceana counties, effective September 15. Dr. Reuben J. Harrington, for fourteen years health officer of Muskegon, has been appointed in charge of the unit in Muskegon County, succeeding Dr. Richard Sears of the state department of health. Dr. Clifton C. Corkill, Ontonagon, director of the Ontonagon-Baraga counties health unit, has been appointed in charge of the Menominee County health department. He succeeds Dr. Lawrence A. Berg, Detroit, who is on a year's leave of absence to take a graduate course at the University of Michigan Medical School.

MINNESOTA

Research in Food Technology.—An annual grant of $25,000 has been given to the University of Minnesota by George A. Hormel and Company, Austin, to establish the Hormel Research Foundation for the promotion of researches in the field of food technology. According to *Science,* most of the research will be devoted to problems of importance to the packing industry. The work will be carried on by a committee consisting of George O. Burr, Ph.D., Ross A. Gortner, Ph.D., Halvor O. Halvorson, Ph.D., Walter M. Lauer, Ph.D., and Samuel C. Lind, Ph.D. Dr. Lind is chairman.

NEW YORK

Free Dispensary Fifty Years Old.—The Syracuse Free Dispensary celebrated its fiftieth anniversary October 13. Rev. Alphonse M. Schwitalla, dean, St. Louis University School of Medicine, was the principal speaker, on "The Future of Dispensaries." Dr. Charles H. Benson, Bainbridge, for many years head of the dispensary and now retired, was a guest of honor.

District Meeting.—The annual meeting of the Fourth District of the Medical Society of the State of New York was held in Amsterdam September 30 and October 1. The speakers included Drs. Lyle A. Sutton, Albany, on "The Menopausal Syndrome"; Stafford L. Warren, Rochester, "Fever Therapy," and William Cook Spain, New York, "The Food Factor in Allergy."

Society News.—Forum discussions made up the program of the Onondaga County Medical Society, Syracuse, November 1. Dr. Brooks W. McCuen led a forum on "Cancer of the Rectum and Colon" with Drs. John C. M. Brust and Albert G. Swift as discussers. Dr. Joseph R. Wiseman led a discussion of "Peptic Ulcer," in which the participants were Drs. Clark J. Laus, Donald S. Childs and Percival K. Menzies. Members of the staff of the Syracuse Psychopathic Hospital presented the program October 4: Drs. Carl A. Whitaker, on "Clinic Treatment of Syphilis of the Central Nervous System" and Eugene Davidoff, "Psychiatric Aspects of the Treatment of Orchidism" and "Play Technic in Children and Juveniles."

New York City

Appointments Available at Hospital for Joint Diseases.—Six house staff appointments on the general service for two years rotating service are available at the Hospital for Joint Diseases, three to begin July 1, 1939, and three to begin Jan. 1, 1940. An examination will be held at the hospital Dec. 29, 1938, for which applicants must register before December 15. The hospital provides maintenance and uniforms. Graduating students and graduates (unmarried men) of class A medical schools are eligible. Applications should be addressed to the Director of the Hospital, Madison Avenue at One Hundred and Twenty-Third Street, New York.

Position Open for Bacteriologist.—The Municipal Civil Service Commission announces a vacancy for a bacteriologist. Applicants must have been citizens and bona fide residents of the city for three years. Requirements are an M.D. degree or a Ph.D. degree in bacteriology from an accredited institution, three years' experience in bacteriology, and in addition two years' specialized training in blood grouping and related serologic work or a satisfactory equivalent. Applications will be received until 4 p. m., November 25. Blanks may be obtained by writing to the commission with return postage enclosed. The address is room 1400, Municipal Building, Manhattan.

NORTH CAROLINA

Symposium at Duke University.—More than 500 Southern physicians attended a symposium on medical problems presented by Duke University, Durham, October 13-15 as the first of a series of symposiums celebrating the university's centennial. After the welcoming address by William Preston Few, LL.D., president of the university, Drs. Allen Weir Freeman, Baltimore, and George W. McCoy, New Orleans, spoke on "Public Health Developments in the South" and "Leprosy in the United States" respectively. In the evening there was a discussion of "The Future of American Medicine" by Drs. Morris Fishbein, Chicago, Editor of THE JOURNAL, John P. Peters, New Haven, Conn., and Wingate M. Johnson, Winston-Salem. Dr. Milton J. Rosenau, professor of epidemiology, University of North Carolina School of Medicine, Chapel Hill, presided. Addresses were presented Friday morning October 14 by Drs. George H. Whipple, Rochester, N. Y., on "Anemia and the Building of Hemoglobin in the Body" and William H. Sebrell Jr. of the U. S. Public Health Service, Washington, D. C., on pellagra. In the afternoon the speakers were Drs. Charles F. Craig and Edward W. Alton Ochsner, New Orleans, on amebiasis and "The Surgeon's Contribution to Treatment of Amebiasis" respectively. The remaining addresses of the symposium dealt also with tropical diseases: Drs. William G. MacCallum, Baltimore, on "Malaria"; Arturo Lorenzo Carrion, University of Puerto Rico School of Tropical Medicine, San Juan, "Rising Significance of Fungus Infections in Man," and Albert M. Snell, Rochester, Minn., "Tropical and Nontropical Sprue (Chronic Idiopathic Steatorrhea): Their Probable Interrelationship." Dr. James Buren Sidbury, Wilmington, president of the Medical Society of North Carolina, presided at the Saturday morning session.

OHIO

The First Lower Lecture.—The first lecture of a series made possible by the establishment of the Lower Fund was presented by Dr. Oliver H. Perry Pepper, Philadelphia, November 18 in the Medical Library Auditorium, Cleveland, on "Diverticulitis of the Colon." Dr. William E. Lower, Cleveland, endowed the lectureship recently, directing that it deal with some recent development or research but not be confined to any one branch of medicine.

Personal.—Dr. John C. Darby, Cleveland, was honored with a dinner September 22 marking his retirement from the 368th Medical Regiment of the Officers Reserve Corps, U. S. Army, of which he had been commander since 1929. He received an honorary life commission as colonel of the regiment. Colonel Darby saw service in the Spanish American War, on the Mexican border and in the World War in France. He was graduated from Western Reserve University School of Medicine in 1900.——Dr. Raymond S. Rosedale, St. Louis, has been appointed pathologist at Mercy Hospital, Canton, to succeed Dr. Max Shaweker.

Society News.—The Morgan County Bar Association entertained the Morgan County Medical Society October 11 in McConnellsville. The speakers were Dr. Roy J. Secrest, until recently assistant medical director of the state industrial commission, on the commission and the practicing physician; Mr. R. H. Edwards, claims referee of the industrial commission, on the expert medical witness, and Dr. William E. Masters, on the doctor as a witness.——Dr. Everett N. Collins, Cleveland, addressed the Portage County Medical Society, Ravenna, September 8, on diseases of the colon.——Drs. Charles A. Doan and Bruce K. Wiseman addressed the Columbus Academy of Medicine September 19 on "Advances in the Understanding, Differential Diagnosis and Treatment of the More Common Anemic States" and "Advances in the Diagnosis and Therapy of Thrombocytopenic Purpura" respectively. ——Dr. William Bates, Philadelphia, addressed the Montgomery County Medical Society, Dayton, November 4, on "Differentiation Between Visceral and Parietal Pain." Drs. Thomas E. Newell and Miles T. Hoerner addressed the society October 7 on "Etiology and Differentiation of Jaundice" and "Surgical Treatment of Lesions Producing Jaundice" respectively.

OREGON

Personal.—Dr. Thomas L. Meador, Portland, has been appointed in charge of the division of communicable disease in the city department of health.

New Orthopedic Club.—Physicians in Portland who limit their practice to orthopedic surgery formed the Portland Orthopedic Club at a meeting October 21. Dr. Otis F. Akin was made president and Dr. Alfred Gurney Kimberley, secretary. Candidates for membership must be diplomates of the American Board of Orthopaedic Surgery.

The Widmer Research Fund.—The University of Oregon Medical School, Portland, has received a gift of 171.67 acres of land near Eugene valued at about $30,000, the income from which is to be devoted to research in cancer and heart disease. The property was conveyed by Misses Gertrude and Margaret Widmer, Eugene, in memory of their parents and of two brothers who graduated from the university. The gift will be established as the Widmer Memorial Research Fund.

Annual Registration Due December 1.—All practitioners of medicine and surgery holding licenses to practice in Oregon are required by law to register annually on or before December 1 with the secretary of the Board of Medical Examiners and at that time to pay a fee of $5. A practitioner failing to register is subject to a penalty of $1 for each thirty days or part thereof of default, and his failure to reregister within ninety days after December 1 is a misdemeanor.

PENNSYLVANIA

Society News.—A symposium on typhoid fever was presented before the Fayette County Medical Society, Uniontown, November 3, by Drs. Charles H. Smith, Herbert Lund and John B. Hibbs, all of Uniontown, and Paul A. Keeney, Harrisburg.——Dr. Morris A. Silver, Harrisburg, addressed the Dauphin County Medical Society, Harrisburg, November 1 on "Recognition of the Commoner Anorectal Diseases and Their Treatment." ——Dr. Daniel Murray Angevine, New York, addressed the Harrisburg Academy of Medicine recently on arthritis.——Dr. Albert F. Doyle, Johnstown, addressed the Montour County Medical Society, Danville, October 21 on "Public Health Duties of the Physician Treating Syphilis."

Pittsburgh

Auxiliary Holds Annual Institute.—The Woman's Auxiliary of the Allegheny County Medical Society held its annual health institute at the William Penn Hotel November 1. Dr. Paul Titus gave an address on maternal conditions in the United States, followed by a showing of the "Birth of a Baby." Dr. Chauncey L. Palmer, chairman of the committee on public health legislation of the state medical society, spoke on "Health Legislation—What State Medicine Means to You." Mrs. Joseph P. Dobo spoke on "State Medicine as I Knew It in Vienna." Dr. John N. Frederick discussed "Mental Diseases with Special Reference to Causes and Prevention," and Dr. William H. Guy presented an illustrated lecture on syphilis.

Society News.—Dr. Claude S. Beck, Cleveland, was the guest speaker before the Allegheny County Medical Society November 15 on "Heart Surgery." A. L. Murray of the U. S. Bureau of Mines, Pittsburgh, addressed the society October 18 on "Carbon Monoxide Poisoning" and Dr. Moses Paulson, Baltimore, "Diarrheas and Dysentery of the Adult —Practical Aspects of Diagnosis and Treatment." The scientific exhibit was presented by the Bureau of Mines. There was also a discussion on "Reaching the Ear of the Health and Tax Conscious Public Through the Membership of the County Medical Society and Its Woman's Auxiliary" by Mrs. Augustus S. Kech, Altoona, chairman of the public relations committee of the Woman's Auxiliary to the Medical Society of the State of Pennsylvania. Other speakers were Drs. Chauncey L. Palmer, chairman of the committee on legislation of the state medical society; Charles H. Henninger, president-elect, and Mrs. Walter F. Donaldson, Pittsburgh, president of the Woman's Auxiliary of the state medical society; all are of Pittsburgh.——Drs. George Booth and Karl Zimmerman addressed the Pittsburgh Academy of Medicine October 25 on "Hypoglycemia" and "Oil Soluble Anesthetics in the Treatment of Anal Ulcer" respectively.

TENNESSEE

District Meeting.—Guest speakers at the annual meeting of the Third Councilor District of the Tennessee State Medical Association in Chattanooga, September 29, were Drs. Hugh H. Trout, Roanoke, Va., on "Some Mistakes in the Diagnosis of Acute Appendicitis" and "Treatment of Carcinoma of the Breast"; Axel N. Arneson, St. Louis, "Carcinoma of the Cervix" and "Carcinoma of the Uterus," and John B. Youmans, Nashville, "Less Common Manifestations of Coronary Thrombosis" and "Recognition of Cardiac Arrhythmias by Simple Physical Examination."

VIRGINIA

Special Society Elections.—Several special societies held their annual meetings in Danville during the annual session of the Medical Society of Virginia in October. The Virginia Orthopedic Society elected the following officers: Drs. Roy M. Hoover, Roanoke, president; Henry H. Wescott, Roanoke, vice president, and Bernard H. Kyle, Lynchburg, secretary, reelected. Dr. William W. Waddell Jr., Charlottesville, was elected president of the Virginia Pediatric Society; Dr. Leta J. White, Petersburg, vice president, and Dr. John M. Bishop, Roanoke, reelected secretary. At the meeting of the Virginia Obstetrical and Gynecological Society the following were elected: Drs. Charles J. Andrews, Norfolk, president; Harry Hudnall Ware Jr., Richmond, vice president, and Richard B. Nicholls, Norfolk, secretary. The Virginia Radiological Society reelected Drs. Frederick M. Hodges, Richmond, president, and Vincent W. Archer, Charlottesville, secretary. Dr. Lawrence T. Price, Richmond, was elected president of the Virginia Urological Society; Drs. Albert A. Creecy, Newport News, and Linwood D. Keyser, Roanoke, vice president and secretary respectively.

WASHINGTON

State Program for Crippled Children.—During the first two years of the state crippled children's program conducted by the Washington State Department of Social Security with state and federal funds, 1,940 children have attended clinics. These clinics have been held at intervals of six months in six centers, and twenty-three orthopedic and plastic surgeons have assisted in them. Of the children, 731 have been referred to the state agency and 309 to private orthopedic units for treatment. The staff surgeons elected from their group seven men to serve as a committee to review cases referred to the crippled children's program and assign them for treatment to the staff surgeons in the hospital center nearest each child's home. The social workers in the hospital centers cooperate in arranging convalescent care and educational facilities. If the child when discharged from orthopedic treatment is of the age of employment but not equipped to enter private industry, he is referred to the state department of vocational rehabilitation for possible training and placement. Since September 1935 the state has spent $118,730.96 in the program and the Children's Bureau contributed $109,354.82.

WISCONSIN

Society News.—Drs. Stanley R. Maxeiner and Henry E. Michelson, Minneapolis, addressed the Barron-Washburn-Sawyer-Burnett County Medical Society in Rice Lake, October 4, on "Surgery of the Stomach and Duodenum" and "Diagnosis and Treatment of Common Skin Diseases" respectively. ——Dr. Raymond G. Arveson, Frederic, president-elect of the State Medical Society of Wisconsin, addressed the Chippewa County Medical Society, Chippewa Falls, October 25, on "Adequacy of Medical Care."——At a meeting of the Grant County

Medical Society, Lancaster, October 25 the speakers were Drs. John C. Grill, Milwaukee, on "Importance of the Laboratory in the Diagnosis of Blood Diseases"; Elmer L. Sevringhaus, Madison, "Menopause and Irregular Menstruation," and George H. Ewell, Madison, "Interesting Urological Cases." Mr. J. George Crownhart, executive secretary of the State Medical Society of Wisconsin, Madison, reported on his recent study of sickness care in Europe.——Dr. Henry W. Meyerding, Rochester, Minn., addressed the Kenosha County Medical Society, Kenosha, September 22 on recent advances in orthopedics.——Dr. James M. Hayes, Minneapolis, addressed the La Crosse County Medical Society October 12 on "Acute Abdominal Surgery" and Dr. Albert E. Rector, Appleton, president of the state medical society, discussed "Present Day Trends in Medicine."

GENERAL

Examinations in Pediatrics. — The American Board of Pediatrics announces that its 1939 examinations will be held April 26 in New York, May 16 in St. Louis, and November 14-15 in Cincinnati. Appointments for the April examinations must be made by December 26, for the May one by Jan. 16, 1939, and for the November one by July 14. The secretary is Dr. Charles Anderson Aldrich, 723 Elm Street, Winnetka, Ill.

The Lilly Award in Biologic Chemistry.—Nominations are invited for the Eli Lilly and Company Prize in Biological Chemistry to be awarded by the American Chemical Society at its spring meeting. The prize, established by the Lilly firm in 1934, is $1,000 with a bronze medal and $150 or as much thereof as is needed to defray the expenses of the recipient to the meeting. A nominee must not be over 35 years old on April 30 of the year of the prize and shall have accomplished outstanding research in biologic chemistry, working in a college or university. For the purpose of this award biologic chemistry does not include immunology, clinical investigation, pharmacology or experimental therapeutics. It is intended for persons on the threshold of their career and will not be judged in comparison with the work of more mature and experienced chemists. Nominations must be received before Jan. 5, 1939. They should be sent directly to the secretary of the American Chemical Society, Charles L. Parsons, Mills Building, Washington, D. C.

Bequests and Donations. — The following bequests and donations have recently been announced:

Christ Church Hospital, Philadelphia, $7,800 by the will of Sarah L. Bailey.

Fitzgerald-Mercy Hospital, Darby, Pa., $5,000 by the will of the late Mrs. May Neff Fitzgerald Major, whose first husband bequeathed funds for the erection of the hospital; Children's Seashore Home, Atlantic City, N. J., also received $1,000.

Mount Sinai Hospital, New York, $10,000 by the will of the late Mrs. Carrie L. Lehman.

Methodist Episcopal Hospital, Indianapolis, $10,000 by the will of Lulu E. Critz, Anderson, Ind., who died June 29.

American Society for the Control of Cancer, New York, $10,000 by the will of Miss Katherine Rhoads, Richmond, Va., to be used in Virginia.

Hamot Hospital Association, Erie, Pa., and Wills Hospital, Philadelphia, $1,000 each by the will of Frank B. Rutherford.

Mansfield General Hospital, Mansfield, Ohio, $25,000 from the estate of the late Richmond Smith.

Lake County Memorial Hospital, Painesville, Ohio, $5,000 from the estate of the late Clifton N. Windecker.

Bronson Methodist Hospital, Kalamazoo, Mich., $100,000 from the Kresge Foundation to be applied on a new addition.

The city of Coshocton, Ohio, will receive about $225,000 from the will of Ernest A. Bachert, to be held in trust for ten years and to be expended at the end of that period for the erection and maintenance of a hospital for crippled children.

Harrisburg Polyclinic Hospital, Harrisburg, Pa., $350,000 by the will of the late Daniel M. Dull in memory of his father.

Society Elections.—Dr. James R. McCord, Atlanta, Ga., was chosen president-elect of the American Association of Obstetricians and Gynecologists at the recent annual meeting and Dr. James E. King, Buffalo, was installed as president-elect. Dr. James K. Quigley, Rochester, N. Y., was elected vice president and Dr. James R. Bloss, Huntington, W. Va., was reelected secretary. The next meeting will be held in Hot Springs, Va.——Dr. Harold D. Corbusier, Plainfield, N. J., was elected president of the Academy of Physical Medicine at the annual meeting in Washington, D. C., in October. Drs. Fred H. Albee, New York, and William H. Schmidt, Philadelphia, were elected vice presidents and Dr. Herman A. Osgood, Boston, was elected secretary. —— Dr. Russell H. Oppenheimer, Atlanta, was chosen president-elect of the Association of American Medical Colleges at its annual meeting in Syracuse, N. Y., October 24-26, and Dr. Willard C. Rappleye, New York, was installed as president. Dr. Waller S. Leathers, Nashville, Tenn., was elected vice president and Dr. Fred C. Zapffe, Chicago, reelected secretary. The next meeting will be held in Cincinnati, Oct. 23-25, 1939.

Radiological Society of North America. — The annual meeting of the Radiological Society of North America will be held in Pittsburgh November 28-December 2 with headquarters at the William Penn Hotel. This year the society is sponsoring its first refresher courses, which will be given November 27-28 in the physics of radiation, radiology of the chest, radiology of the gastrointestinal tract, pathology of tumors, radiology of bone tumors, roentgen analysis of fractures, and radiology of sinuses and mastoids. Much of the scientific program is in the form of symposiums. Among the speakers will be:

Drs. Marcy L. Sussman and Leopold Jaches, New York, Bone Changes in Generalized Lipoid Diseases.

Drs. Ross Golden and Paul C. Swenson, New York, Experiences with the Compression Technic in Gastrointestinal Examinations.

Dr. Milton Friedman, New York, The Relation of Ovarian Hormones to Benign Breast Hyperplasia and Neoplasia.

Dr. Vincent C. Johnson, Ann Arbor, Mich., The Value of Roentgen Examination of the Paranasal Sinuses.

Drs. David E. Ehrlich and Arthur B. Robins, New York, Group X-Ray Surveys of Apparently Healthy Individuals.

Dr. Herman A. Osgood, Boston, Treatment of Acute and Chronic Inflammatory Conditions by Fractional Doses of X-Rays.

Dr. John D. Camp, Rochester, Minn., Experiences with Lipiodol in the Localization of Lesions Associated with Low Back and Sciatic Pain.

Dr. Arthur U. Desjardins, Rochester, Minn., Roentgen Therapy for Chronic Infectious Arthritis.

Dr. Hugh M. Wilson, New Haven, Conn., Exploration of the Thorax with Body Section Roentgenography.

Dr. Henri Coutard, Chicago, Present Conception of Treatment of the Larynx.

Changes in Status of Licensure.—The Ohio State Medical Board recently reported the following action:

Dr. Charles R. Buck, Cincinnati, license restored July 19.
Dr. Ralph Bernard Brown, Columbus, license restored April 5.

The New York State Board of Medical Examiners has recently reported suspension of licenses of the following physicians on the basis of fraud and deceit:

Dr. Isadore Roth, Brooklyn, one year from June 17.
Dr. Benjamin M. Wax, New York, one year from June 17.
Dr. Peter Kleinkopf, New York, eight months from June 17.
Dr. Isidore E. Kaplan, New York, one year from June 17.
Dr. Harry Grodzicker, Brooklyn, one year from June 17.
Dr. Max Ehrenberg, New York, one year from June 17.
Dr. Jacob R. Firneno, Brooklyn, six months from June 17.

The state board of medical education and licensure of Pennsylvania recently reported the following:

Dr. Arthur H. Gaston, Pittsburgh, license revoked for unethical conduct.

Dr. Harry Emerson Gray, Zelienople, license revoked for unethical conduct. It is said that although he had been a general practitioner for many years he posed as an eye specialist for an optical company.

The state department of registration of Utah reports the following action:

Dr. Afton M. Livingston, Ogden, license suspended August 1 for unprofessional conduct; to be reinstated in one year on condition that he complete a graduate course in a medical college.

The Florida State Board of Medical Examiners reports the following:

Dr. Roy Webb, Delray Beach, license restored June 13.

Government Services

Examination for Position of Toxicologist

The U. S. Civil Service Commission announces that an open competitive examination will be held for the position of principal industrial toxicologist (organic compounds) in the U. S. Public Health Service at a salary of $5,600 a year. The duties will be to serve as scientific head of a section of industrial toxicology, studying the relation between chemical composition and pharmacologic action of organic compounds, and to be responsible for the planning and direction of scientific research and routine work in the industrial toxicology of organic compounds. Candidates must have graduated with an M.D. degree from a medical school of recognized standing and must not have passed their fifty-third birthday on the date of the close of applications. Applications and further details may be obtained from the Secretary, Board of U. S. Civil Service Examiners, at any first class post office, from the commission at Washington, D. C., or from the district office of the commission in any of the following cities: Atlanta, Boston, Chicago, Cincinnati, Denver, New Orleans, New York, Philadelphia, Seattle, St. Louis, St. Paul, San Francisco, Honolulu, Balboa Heights, C. Z., and San Juan, P. R. The closing date for applications is November 28, if received from states other than Arizona, California, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington and Wyoming. For the Far Western states the date is December 1.

Foreign Letters

PARIS

(From Our Regular Correspondent)

Oct. 22, 1938.

Action of Ephedrine in Acute Pancreatitis

At the July 8 meeting of the Société médicale des hôpitaux of Paris, a paper was read by Dr. P. Jacquet and his associates on three cases presenting a syndrome commonly observed in the initial stage of an acute pancreatitis. The existence of such an acute pancreatitis was verified at operation in two of the three cases. The clinical picture was identical, the noteworthy features being severe epigastric pain radiating toward the back, which could not be relieved by relatively large doses of morphine. The patients were pale and appeared to be in a state of shock with only slight increase in the pulse rate and no change in the blood pressure. There was a noticeable increase in the blood sugar content and a marked glycosuria in one patient. Ephedrine was given to all four patients to combat the symptoms of shock. In the first case 0.04 Gm. was given daily for three days and was followed by considerable relief of the pain. This patient was operated on successfully later for a hemorrhagic cyst of the pancreas. In the second case the symptoms of acute pancreatitis were accompanied by a hemorrhagic pleurisy. After a few days administration of 0.08 Gm. daily of ephedrine hydrochloride the abdominal pain, shock and pleurisy disappeared, but the pain recurred as soon as the ephedrine was discontinued. After the first dose was repeated the pain ceased. This patient was given a total of almost a gram of ephedrine hydrochloride in twenty-five days and never had a recurrence of symptoms during a year of observation. The third patient was given 0.04 Gm. of ephedrine hydrochloride in a single dose six hours after the onset. The pain and symptoms of shock disappeared but recurred two hours later. A second injection was given thirteen hours after the onset and again gave relief for two hours. A suprapubic incision revealed a hemoperitoneum but the patient's condition did not permit exploration of the upper portion of the abdomen. Recovery followed and no relapse was observed during the next three months. The conclusions based on these observations were that, before the irreparable lesions incident to an acute pancreatitis appear, there is a vascular disturbance on which such factors as the pharmacodynamic action of ephedrine, the shock of an operative intervention or perhaps a general anesthesia seem to have an inhibitory action. Ephedrine ought to be given in much larger doses in acute pancreatitis than in collapse or surgical shock. In the discussion, Dr. Gilbert-Dreyfus cited a case in which operation based on the diagnosis of acute peritonitis revealed an edema of the pancreas. Following the operation, repeated emesis and a poor general condition but no signs of circulatory collapse were noted. The patient was given 0.06 Gm. of ephedrine hydrochloride followed by complete transformation of the clinical picture after the fourth injection. Dr. Donzelot believed that pancreatic lesions were not always responsible for such a severe syndrome. The striking features in the pancreaticosolar syndrome were severe lumbar pain and very marked symptoms of shock.

Prolongation of Effects of Tetanus and Diphtheria Antitoxins

Prof. G. Ramon of the Pasteur Institute of Paris has studied the action of tetanus and diphtheria toxoids since his discovery of both these toxoids about ten years ago. At the July 8 meeting of the Société médicale des hôpitaux of Paris, Prof. Ramon and associates presented the results of the comparative effects of these toxoids in the form of two papers. They recalled their experience in the combined use of the tetanus antitoxin and toxoid in vaccination against tetanus, a method now obligatory in the French army. The person to be vaccinated is given in two different places of the body a dose of the serum, for adults, representing from 10 to 20 thousand antitoxic units and another of 1 cc. of tetanus toxoid. Fifteen days later, 2 cc. of the toxoid is given and again three weeks after the second dose a third one of 2 cc. of the toxoid. The immunity conferred by the antitoxin is thus greatly prolonged. This combined use of the tetanus antitoxin and toxoid was utilized in the treatment of four cases of injuries as a prophylactic measure, the theory being that the serum, owing to its high titer in antitoxic units, had a better immediate protective action but that, because such action was only transitory, it could be prolonged by giving the tetanus toxoid. Each patient received a dose of the serum corresponding to 150,000 units and at the same time he was given 2 cc. of the tetanus toxoid. Later on, doses of 3, 4 and 5 cc. of the toxoid were given at intervals of a few days. Determinations of the antitoxin content of the blood made at various periods showed that it was possible to prolong the passive immunity conferred by the antitoxic serum, which is only of brief duration, by the active immunity due to the toxoid, which after repeated injections becomes more and more permanent. The great advantage of such a combined use of the antitetanus serum and tetanus toxoid is that not only will it be possible to avoid, in the future, the continued administration of large doses of the serum to prevent a late tetanus but the antitoxin units in the blood will be maintained at a sufficiently high titer, when the passive but transitory action of the serum is prolonged, through the active immunizing action of the toxoid. Up to the present, no untoward effect of the use of the toxoid has been reported.

In the second paper Professor Ramon discussed the first results of combined use of diphtheria antitoxin and toxoid. Although the use of the diphtheria antitoxin had revolutionized the treatment of the disease, the effects of the antitoxin in diphtheria conferred only a passive immunity of relatively short duration, so that it has become necessary to repeat the injections in order to prevent serious complications and recurrences. The object which Ramon had in mind in advocating the combined use of the diphtheria antitoxin and toxoid was to avoid giving additional doses of the former. Two injections are given in different parts of the body, one of a massive dose of the antidiphtheria serum, in general from 1,000 to 2,000 units per kilogram of weight, according to the severity of the case, a total of from 10 to 60 thousand units except in very grave cases, in which a dose of 80 thousand units is given. The dose of diphtheria toxoid should be 0.1 cc., representing 150 units. Following this large initial dose of the diphtheria antitoxin, the toxoid is injected at intervals of five days in progressively increasing doses, beginning with 1 cc., then 2 cc., 3 cc. and so on. This technic has been used by various clinicians in 120 cases of diphtheria with but slight reactions to be ascribed to the injections of the toxoid. Only three slight and transitory paralyses of the soft palate have been observed. A study of the titer of antitoxin units in the blood of these patients has shown that the transitory passive immunity conferred by the diphtheria antitoxin is converted into a prolonged active immunity as the result of the action of the toxoid.

In the discussion of the second paper, fifteen cases treated by this method were reported by Professor Debré and Dr. Mallet, who stated that their observations as to the transition from a passive immunity of short duration conferred by the diphtheria antitoxin to the prolonged active immunity conferred by the anatoxin entirely corroborated the report made by Professor Ramon. The number of cases, only fifteen, thus far treated was too small on which to base any opinion. Although no postdiphtheritic paralysis had been observed, the cases had been of a mild type. The allergic reactions due to the use

of the toxoid had been slight. Dr. Marquezy doubted whether Ramon's method offered any real advantages because nearly all patients who have been given the antitoxic serum show a protective titer of antitoxic units in the blood. The most important question in the treatment of diphtheria was to create as large a number of antitoxic units in the blood as possible and at as early a stage as it could be accomplished.

Basal Metabolism in Leukemia and Splenomegaly

Two papers on basal metabolism in leukemia and splenomegaly were read at the July 8 meeting of the Société médicale des hôpitaux by Drs. Emile Weil, hematologist, and A. Aschkenasy. In fifteen cases of leukemia, five of which were of the myelogenous and ten of the lymphatic type, a persistent increase in the metabolic rate, which varied from 50 to 60 per cent, was observed in all the patients. This increase is independent of the number of red blood cells and the percentage of immature forms of red blood cells as well as of the size of the spleen or of the lymph nodes. The increased rate of basal metabolism is the expression of the entire leukopoietic process of the organism. A severe concomitant anemia appears to counteract the effects of the leukemia by lowering the metabolism rate. Although the latter may not have any prognostic value in the leukemias, it is of diagnostic interest in the cryptoleukemias involving the lymph nodes or spleen, in which the metabolic rate is constantly high. They had never observed any beneficial influence from irradiation of the thyroid.

As to the metabolic rate in splenomegaly, only a slight increase was noted in four cases of congenital hemolytic icterus, but a more marked increase in hypertrophic cirrhosis of the liver with splenomegaly. In three cases of Gaucher's disease and even in most cases of isolated splenomegaly, especially those of tuberculous or syphilitic origin, the metabolic rate was found to be about normal as opposed to the increased rate found in splenic cryptoleukemias and in splenohepatomegaly as observed in the erythroblastic form of adults. The rate was considerably increased in both of these types of blood disease. Whenever a high metabolic rate is accompanied by splenomegaly without icterus or acute posthemorrhagic anemia, the clinician must keep in mind the possible existence of a leukemia or of an erythroblastosis. Following splenectomy, a decrease of the metabolic rate was observed in three of four patients and an increase in a fifth one. The authors were of the opinion that the spleen has a constant influence on the metabolic rate but that this influence is subject to variations in individual cases.

BERLIN

(From Our Regular Correspondent)

Oct. 10, 1938.

The Pathology of Poliomyelitis

Dr. Peters of Munich had the opportunity to study the central nervous systems of thirty-nine persons who had died of poliomyelitis in 1937. Poliomyelitic changes were observed in the anterior horns of the spinal cord, in the lateral and posterior horns, in the region of the sensory and vegetative nuclei of the medulla and the pons, in the mesencephalon, in the hypothalamus, in the cerebellum and in various parts of the cerebral cortex (ascending frontal convolution, parietal cortex, insular cortex). In the ascending frontal region pathologic changes had occurred in all the layers, not merely in the third, fourth and fifth layers. In a few cases circumscribed foci, confined to the molecular layer of the frontal central cortex, were observed. Alterations were present throughout the central nervous system: ganglion cells were destroyed and glial-mesodermal infiltrates had formed. The degeneration of ganglion cells was most remarkable in the frontal horns of the spinal cord. In the cadavers studied the substantia nigra was relatively free from pathologic processes; in only a few instances had destruction of ganglion cells taken place therein. This observation is of twofold practical significance: first, it is important to the anatomist for differential diagnosis of poliomyelitis and lethargic encephalitis (Economo) and it is important to the clinician, as he need not fear in general the manifestation of parkinsonian symptoms in persons who have recovered from poliomyelitis. In several cases thick glial-leukocytal infiltrates were found in the pons and in addition a deficiency of ganglion cells at the base of the pons in the vicinity of the pontile nuclei and the area of the pyramidal tract. These foci, together with foci in the ascending central region of the cerebral cortex, can through stimuli or trophic disturbances in the first motor neuron lead to spastic symptoms such as exaggerated reflexes. The latter symptom is more often determined in clinically examined cases. In three cadavers a manifest preponderance of pathologic changes in the brain, especially in the pons and medulla, as contrasted with the spinal cord, were noted. It may be assumed therefore that some cases of poliomyelitis, at least in the initial stage, present only lesions in the cerebral nerves, whereas not the slightest degree of paralysis is present in the region of the extremities; under certain circumstances spastic symptoms may even appear. In a few cases also more or less extensive primary foci were observed in the white substance of the spinal cord. The meningeal lesions, which in some instances consisted of a pronounced maculating, leukocytic meningitis, were interpreted as a primary reaction to poliomyelitis virus and its toxin. An interdependence of the meningeal changes and those in the nerve tissue does not exist; it is a question of coordinated processes. The wide distribution of the pathologic changes in poliomyelitis argues against use of the designation "poliomyelitis anterior." Heine-Medin disease is a myelo-encephalomeningitis which cannot rightfully be qualified by the adjective "anterior."

Sugar and the Teeth

Dr. Wohinz discusses the interrelation of sugar and the teeth in the *Zahnärztlichen Mitteilungen*. Statistics have revealed the astonishing fact that Germany, although a large producer of beet sugar, ranks fifth among the nations as a consumer of sugar. The view that sugar damages the teeth is no longer tenable on the basis of recent observations. Laboratory experiments as well as observations in vivo show that raw sugar and even mixtures of raw sugar and fat (whipped cream, marchpane) and protein exert no corrosive effect on the dental enamel. The injurious effect of neutral yeasty bakery goods can be favorably offset or abolished by ingestion of fruits and vegetables or salads. Carbohydrate ingested in the form of sugar ferments not at all or only as lactic acid. On the contrary, carbohydrate decomposes if ingested in the form of starches; it is first decomposed into sugar by the oral secretions and then undergoes further changes which exert a more harmful influence on the dental enamel than lactic acid. Dental caries among bakers is a special instance; particles of flour and sugar are inhaled in the course of the work; these particles light on the front teeth, and the deposits on the upper jaw in particular are not carried away by the saliva. Workers in sugar are consistently free from sugar caries.

Prof. Johannes Lange Is Dead

With Prof. Johannes Lange, ordinarius in psychiatry at Breslau, passes at the age of 47 one of the finest of the younger German psychiatrists. Lange was a pupil of Kraepelin in the best sense of the word; he was loyal to his teacher and possessed the latter's eagerness for achievement. Lange's energetic pursuit of research and his remarkably able presentation of material quickly smoothed the path of his academic career; at the age of 40 he was already ordinarius. In addition to his particular specialty, Lange concerned himself professionally with cerebral pathology and genetic research and contributed notably to those fields. One has only to recall his research on twins, studies which resulted in the volume "Crime as Destiny." Precisely in this controversial field of genetic research, in which at present

so many differently minded elements are mixed, Lange has accomplished much good through public criticism of exaggerations and spurious representations, no mean task in view of the difficult situations often encountered in this field today.

AUSTRALIA

(From Our Regular Correspondent)

Oct. 12, 1938.

Prophylaxis of Gas Gangrene

A material suitable for immunizing man against gas gangrene due to Bacillus welchii has been described by Penfold and Tolhurst at the Baker Institute, Melbourne. These workers have previously described the immunization of animals with alum-precipitated formaldehyde toxoid made from Bacillus welchii toxin, and their experiments with animals have been so successful that in August 1937 it was decided to use the vaccine in man. An eighteen hour culture of Bacillus welchii grown in anaerobic veal broth containing 0.1 per cent of dextrose was filtered through a Seitz bacterial pad and the minimum lethal dose of the filtrate was determined intraperitoneally in mice. About 0.4 per cent of solution of formaldehyde was added to a freshly prepared toxin and the mixture was incubated at 37 C. for six or seven days, until the toxicity was so reduced that 1 cc. would not kill mice weighing 20 Gm., while 5 cc. would kill rats weighing 100 Gm. The toxoid was precipitated with an 8 per cent solution of alum and the immunizing power of the material was tested in guinea pigs. The first human subject received 0.25 and 0.5 cc. subcutaneously, with an interval of four weeks between the doses. The reactions were mild and restricted to the site of inoculation. Further injections in different persons with doses up to 1 cc. caused no serious reactions. Examination of immunity response showed that this alum-precipitated Bacillus welchii toxoid given in two or three injections stimulated the production of antitoxin in all the persons injected. To demonstrate that the immune human serum was fully protective against living Bacillus welchii culture, passive immunity experiments were carried out in mice. It was found that the protected mice withstood at least two minimum lethal doses of culture. It has not yet been determined what level of antitoxin is fully protective or what is the duration of the immunity in man.

Physical Fitness Campaign

Australia has lagged behind certain other countries in attempting to improve the health and physique of her people by engaging in an intensive campaign of public education in physical fitness. It is encouraging that several of the state governments have taken steps this year in such a direction. At a meeting of the delegates from sporting bodies with a commonwealth-wide representation held in Sydney following this year's Olympic Games, it was agreed that there was urgent need for a fitness campaign in Australia. This feeling coincides with a similar development in medical and scientific circles, and plans for the institution of such a campaign is now under consideration in most states. One difficulty is the scarcity of qualified instructors who are fully acquainted with modern methods in physical training now in practice abroad. A welcome indication of progress is the appointment of a Canadian expert to the position of director of physical education in New South Wales, which state is furthest advanced in the fitness movement. Its government has appointed a physical education advisory committee to recommend methods adapted to local circumstances and the character and ideals of the community which can be adopted in New South Wales. It is hoped that sporting organizations, medical societies and other scientific bodies will cooperate fully in this movement which has found life in Australia this year. Fortunate as we are in the matter of low death rates and facilities for enjoying the benefits of open air games, there is manifest scope for the avoidance of much sickness which would yield to a better understanding by the people of the functioning of their bodies.

Insurance Difficulties in New Zealand

New Zealand, as well as Australia, is experiencing some difficulty over the question of cooperation between the medical profession and the government on matters pertaining to health insurance. The British Medical Association in New Zealand, feeling that the government's proposed scheme for a universal practitioner service offered no appreciable advantage over the system that obtains at present, submitted to the government an alternative scheme for a more complete service based on income limits. The New Zealand government rejected this scheme, and as a result the association has broken off all discussions with the government. This difficulty with the medical profession is not the only problem met by the government in its attempt to introduce its social security plan. For several months a special committee has been investigating financial aspects of the whole scheme, without reaching any satisfactory decisions.

Tests of the Milk Supply

The announcement that, in future, regular monthly bacteriologic tests will be made of Melbourne's milk supply marks a progressive step in the development of Australia's public health activities. This is the first regulation of its kind in Australia. Under the plan, milk from every farm supplying the metropolitan area will be subjected to a test once a month. The work will be carried out by officers of the department of agriculture, the cost being met by the milk board. These tests will give metropolitan consumers definite assurance of a clean and safe milk supply, and it is expected that this assurance will stimulate the consumption of milk—a result desirable from the medical as well as the producers' standpoint, as the consumption of milk in Australia, notwithstanding the fact that dairying is one of its most important industries, is far below an adequate requirement for optimal health.

Gift for China

The Australian government has provided 500,000 doses of anticholera serum as part of a world gift of 6,000,000 doses to aid China in fighting her present epidemics of cholera. The serum was prepared by the commonwealth laboratories and is valued at approximately £4,000.

Death of Sir Colin MacKenzie

The death of Sir William Colin MacKenzie, M.D. (Melbourne), F.R.C.S. (Edinburgh), F.R.S. (Edinburgh), the founder and first director of the Australian Institute of Anatomy at Canberra, means a definite loss to the medical profession of Australia. Sir Colin belonged to that small band of Australian medical men whose work and writings are known beyond the confines of our island continent. He had a most unusual professional career, graduating as a comparative anatomist from the ranks of general practitioners of medicine. One of his earliest studies was on syphilitic dactylitis, and for two years before Schaudinn's momentous discovery of the spirochete of syphilis he urged the officers of the bacteriologic department of the University of Melbourne to collaborate with him in a search for the causal organism. During his first visit to Europe in 1904, MacKenzie was greatly influenced by the principles of muscle rest and muscle recovery then finding a place in orthopedic treatment. On his return to Melbourne the treatment of the recent and remote effects of infantile paralysis on children was the master idea in his mind. He gradually evolved his theories relating to the fascinating subject of muscle reeducation. These slowly took shape until they were ultimately embodied in his textbook "The Action of Muscles, Including Muscle Rest and Muscle Reeducation." Although commonplace today, MacKenzie's original concep-

tions were then revolutionary. He was the first to use the special term "muscle reeducation" and to stress the importance of the action of gravity in all educational attempts to regain muscle function after paresis of any nature. The minimal load, the zero position, the smooth powdered surface of board or cardboard for reeducational muscle work must always be associated with his name. While an orthopedic surgeon he found time to investigate the special anatomic problems associated with native fauna in Australia. These dissections helped him to correlate function and structure in muscles and to develop treatment for paralyzed muscles accordingly. After the great war MacKenzie devoted himself more and more to comparative anatomy, and his collection of Australian faunal specimens eventually became too great for any private individual. The commonwealth government acquired the collection as a gift to the nation in 1924. Subsequently William Colin MacKenzie received the honor of knighthood. In 1930 the collections were transferred to Canberra and have since been housed, with many additional gifts, in the two spacious museums attached to the Australian Institute of Anatomy. Here, as director, Sir Colin spent the remainder of his working life. His services to Australia will become of more and more importance as research workers of the future make use of the material that he made available to them.

BELGIUM

(From Our Regular Correspondent)

Oct. 8, 1938.

Benzenes, Benzines and Industrial Safety

Mr. A. Stassens has had published in *Industrie chimique belge* a noteworthy report on the medical aspect of the problem of benzenes (C_6H_6, or benzol), benzines (European industry calls the American "gasoline" also "benzine") and industrial safety; a discussion of all aspects, chemical, technical, professional, of the industrial use of hydrocarbons is included. Around 1936 a large number of serious cases of benzene poisoning were reported in various Belgian industries. Following these incidents, investigations were begun and Mr. Stassens collected a great deal of interesting information. The first part of the report is devoted to the benzene compounds (production, rectification, properties, utilization, methods of analysis). All relevant practical data with regard to the toxicity of these products is set forth. The second part of the report deals with the "benzines," substances which are still all too frequently confused with the benzene compounds. The author discusses the production of benzines, the refining process, the physical and chemical determinations used in analyses, the toxicity. All these points are the object of a detailed and careful study. In a third section of his report, Stassens discusses the problem of those closed chain compounds which, by their presence in essences of petroleum, impart formidable toxic properties to the latter. An appendix to the report contains the texts of all pertinent legislation. Physicians will read with interest this clear, complete and accurate portrayal of the contemporary question of hydrocarbons. They will simultaneously become convinced of the complex nature of the problem and of the need for active participation of doctors, as well as industrialists and workers, in the protection of that ever increasing number of persons in industry who are exposed to this particularly serious and fearful type of poisoning.

Yellow Fever in the Belgian Congo

Dr. Van Campenhout recently published a study on yellow fever in the Belgian Congo. A continuous and energetic crusade against Aedes aegypti, which is the main transmitting agent of the virus in epidemics in urban centers, is carried on. The sanitary conditions have been improved to such an extent in Matadi that the use of mosquito netting is no longer necessary. The examination of samples of liver tissues which were taken from cadavers in all suspected cases of yellow fever has not given, up till now, confirmation of the presence of the disease. Further examinations will be made on tissues taken from viscerotomy in new cases. Reports have been made on the communications recently passed to the International Office of Public Health. The head physician of the colony has not believed it his duty, up till now, to encourage the administration of anti-yellow fever vaccines although some volunteers asked to have them administered. There are many donors of immunizing serum. Disinfection of air ships in the Belgian Congo by the use of pyrethrum preparations has given satisfactory results. Fumigations are made just before embarkment and departure of the ship. The sanitary aerodromes of Leopoldville and Coquilhatville are provided with means against yellow fever. Elisabethville, Libenge and Boma aerodromes can be provided for this purpose in a few days if necessary.

Professional Secrecy

An interesting discussion of professional secrecy was made by Dr. Heger in the Société de médecine légale of Belgium. The author called to mind a series of authoritative opinions with regard to the ethics to be maintained by physicians who also serve as officials of public or private organizations. He summarized his own views by saying that professional secrecy is unqualifiedly *de rigueur* for the practitioner who serves in an official capacity. The attending physician may furnish a certificate to a patient on request, but he is under no compulsion to do so. Dr. Ilivier asked the society's opinion on the following point: A medical expert is appointed by a court of law to ascertain the cause of death in an industrial accident case. For the fulfilment of his mission he must be in possession of all pertinent facts. Ought the attending physician to communicate his medical record of the accident victim to the medical examiner? Dr. Duvoir formally replied in the negative and cited a 1913 decision of the Court of Cassation, which holds that a criminal violation of medical secrecy has been committed as soon as the information has been divulged and regardless of the presence or absence of malicious intent. According to Dr. Duvoir the best procedure for a medicolegal expert to follow in general is this: The expert should advise the interested party to request of the injured person's physician a detailed certificate which the injured person could then submit to the expert. Dr. Daubrow objected that in the event of the patient's decease the claimants would have the status of third parties, and certificates delivered to third parties become *ipso facto* null and void. Under such circumstances an insurance company would be able to allege the incompetence of any certificate produced. Although a convinced upholder of professional secrecy, Dr. Daubrow could not help but admit that in certain cases the observance of secrecy may hamper the elucidation of the truth.

Marriages

PAUL HARDIN HARMON to Miss Mary Logan Coleman, both of Springfield, Ill., September 13.

PAUL L. BERGSTROM, Kirkland, Ill., to Miss Lyne Gruhn of Columbus, Wis., September 4.

LIONEL GATES, Coalport, Pa., to Miss Mary H. Ryan of Mahanoy City, September 25.

HAROLD HENRI KLINGER, Akron, Ohio, to Miss Lucie Pickett of Fitzpatrick, Ala., recently.

MYRON REESE BAUMGARTNER to Miss Helen Berg, both of Dalton, Ohio, September 18.

WILLIAM T. DAILY, Brooklyn, to Miss Beatrix K. Robinson of New York, September 6.

HORACE F. BURTON, East Tawas, Mich., to Miss Helen Koth of Bay City, September 17.

ROBERT WILLIAM GRAVES to Miss Anne Yates, both of Durham, N. C., September 7.

REGINALD G. JOHNSTON to Mrs. Doris Greenwood, both of Medina, Ohio, recently.

Deaths

John Lawrence Yates ⊕ Milwaukee; Johns Hopkins University School of Medicine, Baltimore, 1899; chairman of the Section on Surgery, General and Abdominal, American Medical Association, 1934-1935; assistant in pathology at his alma mater in 1901; assistant demonstrator of pathology at the University of Pennsylvania, Philadelphia, from 1902 to 1903; practiced in Milwaukee since 1906; member of the American Surgical Association, Society of Clinical Surgery and the American Association for Thoracic Surgery; fellow of the American College of Surgeons; served during the World War; consulting surgeon to the Milwaukee County and Milwaukee Children's hospitals, and attending surgeon to the Columbia Hospital; at one time on the staff of the Augustana Hospital, Chicago; aged 65; died, November 3, of a throat infection.

Louis Marshall Warfield ⊕ Milwaukee; Johns Hopkins University School of Medicine, Baltimore, 1901; member of the Association of American Physicians; fellow of the American College of Physicians; served during the World War; at one time associate professor of pathology, Milwaukee Medical College, professor of clinical medicine, Marquette University, instructor and lecturer on clinical chemistry and microscopy, Washington University Medical School, St. Louis, and professor of internal medicine at the University of Michigan Medical School, Ann Arbor; on the staffs of the Columbia, Evangelical Deaconess and Milwaukee County General hospitals; aged 62; was found dead in his automobile, September 28, of a bullet wound.

John William Powers ⊕ Milwaukee; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; clinical professor of orthopedic surgery, Marquette University School of Medicine; member of the Clinical Orthopedic Society and the American Academy of Orthopedic Surgeons; fellow of the American College of Surgeons; served during the World War; orthopedic surgeon to the Milwaukee County, St. Joseph's and Marquette University hospitals; aged 57; died, September 29, of arteriosclerosis.

Adolf Gunderson ⊕ La Crosse, Wis.; Koneglige Frederiks Universitet Medisinske Fakultet, Oslo, Norway, 1890; fellow of the American College of Surgeons; formerly member of the board of health; on the staffs of the La Crosse, Lutheran and St. Francis hospitals; at one time regent of the University of Wisconsin, Madison; aged 72; died, September 15, in Norway of bilateral nephrolithiasis, uremia and pyelonephritis.

Harry Thomas Upshaw ⊕ Pasadena, Calif.; St. Louis University School of Medicine, 1915; assistant clinical professor of surgery, University of Southern California School of Medicine, Los Angeles; fellow of the American College of Surgeons; on the staffs of the Huntington Memorial Hospital and the Los Angeles County Hospital; served during the World War; aged 46; died, August 12, of coronary thrombosis.

Grafton Burke ⊕ Fort Yukon, Alaska; University of the South Medical Department, Sewanee, Tenn., 1907; an Associate Fellow of the American Medical Association; fellow of the American College of Surgeons; for many years a medical missionary; medical director of the Hudson Stuck Hospital; aged 56; died, September 25, in the Virginia Mason Hospital, Seattle.

Frank Wade Robertson, New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1895; member of the American Psychiatric Association; at one time medical superintendent of Stamford (Conn.) Hall; formerly senior physician and superintendent of the Elmira (N. Y.) Reformatory; aged 69; died, August 27.

William Howard Halsey, San Diego, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; for many years a surgeon in the U. S. Navy; served during the World War; formerly on the staff of St. Mary's Hospital, Milwaukee; aged 54; died, August 14, of coronary thrombosis.

Frank W. Hendley, Cincinnati; Medical College of Ohio, Cincinnati, 1885; veteran of the Spanish-American and World wars; formerly medical officer and member of the claims board of the U. S. Veterans Bureau; medical director of the Cincinnati Mutual Life Insurance Company; aged 78; died, September 12, in the Christ Hospital.

Alfred Careno Croftan ⊕ Chicago; Hahnemann Medical College and Hospital, Chicago, 1896; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1898; at one time on the staff of St. Mary of Nazareth Hospital; aged 67; died, August 22, in Pasadena, Calif., of carcinoma of the colon.

Robert Hollingsworth Potts ⊕ New Orleans; Tulane University of Louisiana School of Medicine, New Orleans, 1918; assistant professor of medicine, Louisiana State University Medical Center; visiting physician to the Charity Hospital and on the staff of the Southern Baptist Hospital; aged 53; died, August 22.

Argal Ernest Hubbard, Oaklandon, Ind.; Chicago College of Medicine and Surgery, 1912; member of the Indiana State Medical Association; medical director and superintendent of the Sunnyside Sanatorium; formerly medical director of the Municipal Tuberculosis Sanitarium, Peoria, Ill.; aged 57; died, September 15.

William Emmet Buehler ⊕ Chicago; College of Medicine and Surgery, Chicago, 1904; Hering Medical College, Chicago, 1906; president emeritus and on the consulting staff of the Illinois Masonic Hospital; diagnostician on the staff of the American Hospital; aged 69; died, September 19, of coronary disease.

William Townsend Dunning, Gonzales, Texas; University of Texas School of Medicine, Galveston, 1909; member of the State Medical Association of Texas; served during the World War; formerly on the staff of the Holmes Hospital; aged 53; died, September 3, in the Nix Hospital, San Antonio.

Pierson B. Peterson, Honesdale, Pa.; Pulte Medical College, Cincinnati, 1891; member of the Medical Society of the State of Pennsylvania; formerly county coroner; at one time on the staff of the Wayne County Hospital; aged 74; died, August 8, of cerebral hemorrhage and arteriosclerosis.

Mary Freyer Montgomery ⊕ San Francisco; University of California Medical School, San Francisco, 1925; assistant clinical professor of surgery at her alma mater; assistant attending staff member, Children's Hospital; aged 39; died, August 30, in the University of California Hospital.

Thomas Micajah Fly ⊕ Little Rock, Ark.; University of Arkansas School of Medicine, Little Rock, 1903; formerly on the faculty of the University of Arkansas School of Medicine as associate in medicine; city health officer; aged 58; was found dead, September 21, of coronary occlusion.

Leslie Ramsey Hazlett ⊕ Butler, Pa.; Jefferson Medical College of Philadelphia, 1896; member of the American Academy of Ophthalmology and Oto-Laryngology; on the staff of the Butler County Memorial Hospital; aged 70; died, August 10, of coronary occlusion.

Jonas Zettlemoyer, Philadelphia; Temple University School of Medicine, Philadelphia, 1914; member of the Medical Society of the State of Pennsylvania; for many years connected with the bureau of public health; aged 75; died, August 9, in the Presbyterian Hospital.

George F. Weber, Ira, N. Y.; College of Physicians and Surgeons, Baltimore, 1889; at one time county coroner; for many years health officer; aged 74; died, August 30, in the Syracuse (N. Y.) Memorial Hospital of coronary thrombosis and diabetes mellitus.

Otto Frederick Aufderheide, St. Louis; Homeopathic Medical College of Missouri, St. Louis, 1900; member of the Missouri State Medical Association; aged 60; died, September 14, in the Christian Hospital, of intestinal obstruction due to intussusception.

William Curtis Cross, Ashtabula, Ohio; Cleveland University of Medicine and Surgery, 1896; veteran of the Spanish-American War; at one time member of the city board of education; aged 65; was killed, September 7, in an automobile accident.

Frank Louis Waite ⊕ Hartford, Conn.; Bellevue Hospital Medical College, New York, 1888; member of the American Ophthalmological Society; aged 72; on the staff of the Hartford Hospital, where he died, August 31, of cerebral thrombosis.

Hugo Alexander, Hoboken, N. J.; Columbia University College of Physicians and Surgeons, New York, 1911; member of the Medical Society of New Jersey; served during the World War; aged 51; died, September 14, of coronary embolism.

Chester Arthur Miller, Thedford, Neb.; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1902; served during the World War; aged 64; died, August 29, in the Mercy Hospital, Council Bluffs, Iowa, of leukemia.

Victor Bychower, Malden, Mass.; Kaiser-Wilhelm-Universität Medizinische Fakultät, Strassburg, Germany, 1888; member of the Massachusetts Medical Society; aged 77; died in September at Bethlehem, N. H., of cerebral hemorrhage.

Giles Edward Harris, Hugo, Okla.; Louisville (Ky.) Medical College, 1905; member of the Oklahoma State Medical Association; served during the World War; aged 60; died in September of injuries received in an automobile accident.

Luther Clarence Neill, Washington, D. C.; George Washington University School of Medicine, Washington, 1904; veteran of the Spanish-American War; aged 61; died, August 10, of rupture of aneurysm of the aorta and arteriosclerosis.

Carl Schumann, Delhi, N. Y.; New York Homeopathic Medical College and Hospital, 1887; member of the Medical Society of the State of New York; aged 75; died, August 2, in the Delhi Hospital of arteriosclerotic heart disease.

Augustus Camillus Connor ✠ Lexington, Texas; University of Louisiana Medical Department, New Orleans, 1883; past president of the Lee County Medical Society; aged 79; died, September 1, of hypostatic pneumonia.

Charles Highsmith, Dunn, N. C.; Baltimore Medical College, 1898; member of the Medical Society of the State of North Carolina; aged 66; died, September 9, in the Highsmith Hospital, Fayetteville, N. C., of pneumonia.

Theodore Edward Schwarz, Oakland, Calif.; Medical College of Ohio, Cincinnati, 1900; member of the California Medical Association; served during the World War; aged 60; died, August 4, of coronary thrombosis.

Gustavus Crocker Simmons ✠ Inverness, Calif.; Harvard University Medical School, Boston, 1885; at one time mayor of Sacramento and president of the board of health; aged 75; died, August 8, of coronary occlusion.

Edward Everett Barbour, Peoria, Ill.; Physio-Medical College of Indiana, Indianapolis, 1899; member of the Illinois State Medical Society; aged 69; died, September 22, of lobar pneumonia and Parkinson's disease.

Rose D. Howe Jameson, Bethlehem, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1891; member of the Connecticut State Medical Society; aged 73; died, August 17, of cerebral thrombosis.

True Deloss Coe ✠ Keithsburg, Ill.; Rush Medical College, Chicago, 1884; past president of the Mercer County Medical Society; aged 78; died, September 7, in a hospital at Monmouth of pneumonia.

Kenneth Franklin Hughes, St. Louis; University of Illinois College of Medicine, Chicago, 1937; aged 29; was killed, September 15, when the automobile in which he was driving was struck by a train.

John G. W. Knoll, Buffalo; University of Pennsylvania Department of Medicine, Philadelphia, 1888; for many years on the staff of the Deaconess Hospital; aged 73; died, August 26, of food poisoning.

Anthony Caputi, Brooklyn; Hahnemann Medical College and Hospital of Philadelphia, 1935; aged 30; on the staff of the Prospect Heights Hospital, where he died, September 5, of pneumonia.

Edward Freeman Walsh, Pasadena, Calif.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1886; aged 80; died, August 31, of diabetes mellitus.

Alberto Garcia de Quevedo, Washington, D. C.; University of Maryland School of Medicine, Baltimore, 1915; aged 45; died, August 29, of cirrhosis of the liver and diabetes mellitus.

James Ignatius Keaney Jr.; St. Joseph, Mo.; St. Louis University School of Medicine, 1906; on the staff of the State Hospital Number 2; aged 62; died, September 9, of cardiac disease.

Harry Samuel Hughes ✠ St. Louis; St. Louis University School of Medicine, 1905; aged 56; was killed, September 15, when the automobile in which he was driving was struck by a train.

William F. Berkenstock, Philadelphia; Hahnemann Medical College of Philadelphia, 1884; aged 76; died, September 5, in Atlantic City, N. J., of arteriosclerosis and aortic stenosis.

William Frederick Imrie Dey, New York; University of Toronto Faculty of Medicine, 1910; served during the World War; aged 56; died, September 16, of heart disease.

Clarence S. Branson ✠ St. Joseph, Mo.; Ensworth Medical College, St. Joseph, 1910; on the staff of St. Joseph's Hospital; aged 50; died, September 16, of coronary thrombosis.

William Herbert Nute ✠ Exeter, N. H.; Medical School of Maine, Portland, 1881; on the staff of the Exeter Hospital; aged 80; died, August 18, of coronary thrombosis.

Thomas Bassett Keyes ✠ Lake Bluff, Ill.; Albany (N. Y.) Medical College, 1895; aged 62; died, October 2, of myocarditis.

Andrew Foster Whitford, Cambridge, Mass.; Baltimore University School of Medicine, 1893; died, August 24.

Correspondence

MEETING OF THE AMERICAN PUBLIC HEALTH ASSOCIATION

To the Editor:—I have just read the interesting editorial on page 1770 of THE JOURNAL of November 5 and also the news item on page 1775 with regard to the action of the American Public Health Association at its sixty-eighth annual meeting at Kansas City, Mo., October 25-28. Every one in attendance at the meeting was very much distressed at the total misconception of the attitude and action of the association by the public press, but we are much more disturbed because of the failure by THE JOURNAL to understand this action. The resolutions speak for themselves. The following resolution was written by Dr. Abel Wolman, the distinguished sanitary engineer of Baltimore, who is president of the association, and was unanimously adopted on motion of Dr. Thomas Parran, Surgeon General of the U. S. Public Health Service:

> The American Public Health Association records its appreciation of the participation in its deliberations during this annual meeting week of Dr. Irvin Abell, President of the American Medical Association. It records with pleasure its agreement with the approval in principle, at a recent special session of the House of Delegates of the American Medical Association, of the content of the National Health program presented by the Interdepartmental Committee to the National Health Conference. The association pledges its continued cooperation and support to the American Medical Association in the translation of this policy into action.

There was no difference of opinion expressed in the Governing Council, which corresponds with the House of Delegates of the American Medical Association; the resolution with regard to the Report of the Technical Committee on Medical Care as published in THE JOURNAL expressed exactly the unanimous feeling of the Governing Council. There was not a single expression made in favor of so-called health insurance and there was no difference of opinion between the medical and lay members of the association. The action was unanimous, the consideration was as constructive and on as high a plane as that of the memorable special session of the American Medical Association in Chicago, and the practical agreement between the American Medical Association and the American Public Health Association should be emphasized, rather than the studied effort to create the impression that there was a division of opinion.

I am sorry that you and every other thoughtful member of the medical profession could not have been present at this meeting, where those who specialized in public health found themselves in practically complete accord with the splendid statement made by Dr. Irvin Abell as President of the American Medical Association.

Following the adoption of the resolution, and the precedent set by the American Medical Association, the following committee was appointed to confer with the Interdepartmental Committee, the American Medical Association, the American Dental Association, the National Organization of Public Health Nurses, the Conference of State and Territorial Health Officers and other agencies: Drs. Abel Wolman, president of the association, as chairman; J. N. Baker of Alabama; Louis I. Dublin, vice president of the Metropolitan Life Insurance Company of New York; Harry S. Mustard of New York; John L. Rice of New York; Felix J. Underwood of Mississippi, and myself. Drs. E. S. Godfrey, president-elect, and Reginald M. Atwater, executive secretary of the association, are ex officio members.

As you know, Dr. Baker, Dr. Underwood and I are members of the House of Delegates of the American Medical Association. The chairman of the Committee on Resolutions was Dr. A. J. Chesley of Minnesota, who is secretary of the Conference of State and Territorial Health Officers and a member of the Committee on Study of Medical Care of the American Medical Association.

I desire respectfully to submit that those of us interested in the preservation of the integrity and traditions of American

medicine can serve it and the American people better by emphasizing the essential unity of all branches of the medical and allied professions in support of the constructive sections of the National Health Program, and in the practically unanimous objection to compulsory health insurance, than by reemphasizing the captious objections raised by individuals in the various organizations.

A. T. McCORMACK, M.D., Louisville, Ky.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

DIVERTICULITIS

To the Editor:—A patient aged 55 has had vague abdominal pains for nearly a year. Most of the pain seems to be in the left lower quadrant. Complete examination is quite normal except for a blood pressure of 166 systolic, 104 diastolic and extreme nervousness. X-ray examination of the stomach, gallbladder and lungs is normal; the electrocardiogram is normal. A barium sulfate enema reveals diverticula in the sigmoid with rather marked spasm at the junction of the descending and sigmoid colon. I have tried many diets and various medications, such as atropine, phenobarbital and bromides. The bowels are not constipated. I would appreciate anything further you may suggest.

M.D., Ohio.

ANSWER.—The abdominal distress is undoubtedly due to the diverticula and associated local spasm. Because of the patient's hyperkinetic state he is more susceptible to pain stimuli. The treatment should consist of a nonresidue diet and an oil retention enema each night of 3 or 4 ounces (about 100 cc.) of olive oil, to which 20 grains (1.3 Gm.) of thymol iodide powder should be added. Antispasmodics should be tried such as novatropine. If these measures fail, an attempt may be made to fill the diverticula with a nontoxic substance. This can be accomplished by giving barium sulfate or bismuth subcarbonate in 2 ounce (60 Gm.) doses once a week for six weeks.

SKIN GRAFT TO FINGER TIP

To the Editor:—When a patient accidentally cuts off the end of the finger tips for from one-fourth to one-half inch, leaving the bone exposed, would it be feasible to use a plaster cast immobilizing the hand and arm to the opposite side of the patient's abdomen and making a graft of the skin from that area to cover the stumps? Will such skin later provide a serviceable practical skin that will stand up satisfactorily under hard physical usage?

M.D., California.

ANSWER.—The immediate covering of such losses, where the wound has been from a clean cut rather than a crushing one, is desirable and the skin of the flank is acceptable. Occasionally, by simply flexing the finger on the hand, a small flap from the hand can be put in place. Still more infrequently it may be possible, if there has been a clean excision of the tip of a finger, to do a free graft provided the tip itself has not been too greatly contaminated. The transplanted skin from any area will not have the characteristic tough padding of the finger tip and may need the protection of a glove if exceptionally hard work is to be done.

ARTHRANOL, ERTRON AND LYXANTHINE-ASTIER

To the Editor:—What information can you give me concerning the following in the treatment of arthritis? (1) Arthranol (*Time*, Sept. 26, 1938); (2) Ertron (Nutrition Research Laboratories, Inc., Chicago); (3) Lyxanthine-Astier (Gallia Laboratories, Inc., New York).

M.D., Brockport, N. Y.

ANSWER.—1. Arthranol, stated to be a mixture containing essentially ammonium phosphate, ammonium iodide, ammonium chloride, ammonium benzoate, ammonium salicylate and water, was discussed editorially in THE JOURNAL October 8, page 1381. It is recommended for use in the treatment of arthritis, but no competent evidence is available to indicate its usefulness.

2. Ertron was the subject of an adverse report of the Council on Pharmacy and Chemistry (THE JOURNAL, July 10, 1937, pp. 132 and 133). It is claimed to be a highly potent vitamin D preparation. The Council found no evidence to establish the value of such preparations in the treatment of arthritis.

3. Lyxanthine-Astier has not been examined by the Council nor has the American distributor, Gallia Laboratories, Inc., requested the Council to consider the preparation for the purpose of determining its eligibility for inclusion in New and Nonofficial Remedies.

According to advertising material distributed by the Gallia laboratories in 1936, Lyxanthine-Astier is a "new product developed by the famous research laboratories of Dr. P. Astier of Paris, France," an "efficient anti-arthritic, antirheumatic" associating "sulphur, calcium and iodine with the potent uric acid solvent, lysidin bitartrate." The following formula appears in the advertising: "Iodo-propanol-sulphonate of sodium 12 grs., bitartrate of lysidin 9 grs., calcium gluconate 12 grs., sodium bicarbonate 37 grs., tartaric acid 15 grs., citric acid 6 grs., powdered sugar 9 grs., oil of lemon, several drops."

Although lysidin is claimed to be the "main active element" of Lyxanthine, in his studies carried out some twenty years ago, Hanzlik reached the conclusion that there is sufficient scientific evidence to indicate the worthlessness of lysidin as a urate solvent (*J. Lab. & Clin. Med.*, February 1917; Report of the Therapeutic Research Committee, 1917). The other active "anti-rheumatic agents" of Lyxanthine are stated to be iodine and sulfur in the form of iodopropanol sodium sulfonate and calcium gluconate. The latter substance has been accepted by the Council for inclusion in New and Nonofficial Remedies as the effective agent for obtaining the therapeutic effects of calcium. However, the Council's publication gives no recognition to claims of usefulness as a treatment for arthritis.

Lyxanthine-Astier appears to be a needlessly complex and unscientific mixture of well known substances marketed under a fanciful name with claims that have not been confirmed by competent investigations.

BILATERAL PHRENICECTOMY FOR TUBERCULOSIS

To the Editor:—Is bilateral permanent phrenicectomy compatible with life where the operations on the two sides are done at long intervals on persons who have adequate functional lung tissue in the upper portions?

M.D., California.

ANSWER.—Not only is bilateral phrenicectomy compatible with life but even simultaneous bilateral phrenic exeresis may be performed without causing visible harm. In dogs, unilateral multiple intercostal nerve paralysis has been performed, in addition, without causing death. W. S. Lemon (*Am. J. M. Sc.* **177**:319 [March] 1929) reported one dog on which he did complete bilateral, intercostal neurectomy and bilateral phrenic paralysis in four stages without death, and without dyspnea except under anesthesia. The advisability of such operations is another matter. Alexander (Collapse Theory of Pulmonary Tuberculosis, 1937, p. 152) says that he has never seen a patient for whom a permanent bilateral phrenic paralysis was indicated. Even temporary bilateral paralysis is rarely performed. Alternating temporary paralysis, however, is not infrequently resorted to, time being allowed for function to return to the side operated on first.

HEMOPHILIA

To the Editor:—A boy aged 16 is a real hemophiliac. Recently I read in the *Lancet* (**2**: 1142-1149 [Nov. 14] 1936, about a supposed aid in hemophilia. The article spoke of mixing egg white with potassium bromide and keeping this mixture in an incubator at body temperature for several days. Then this mixture was injected for treatment of the blood condition. Is there any scientific basis for this mixture doing any good?

J. H. BURROWS, M.D., Williamsport, Pa.

ANSWER.—Recent research in hemophilia has been directed toward a study of the blood serum. The investigations of Patek and Taylor (*J. Clin. Investigation* **16**:133 [Jan.] 1937) and of Pohle and Taylor (*ibid.* **16**:741 [Sept.] 1937) have suggested that in hemophilia there may be a deficiency in certain serum globulins. They have shown that a globulin substance prepared from normal human serum accelerates clot formation of hemophilic and normal blood but that hemophilic blood serum lacked this property. A similar theory is suggested by the studies of Eley, Green and McKhann (*J. Pediat.* **8**:135 [Feb.] 1936) and of Bendien and Greveld (*Acta. brev. Neerland.* **5**:135, 1936) on the effects in hemophilic patients of human placental extract, which may contain a similar globulin substance.

There may be some relation between these studies and those of Timperley, Naish and Clark referred to in the question. These authors report that repeated injection of an extract prepared from egg white reduces the clotting time and controls hemorrhage in hemophilic patients. The apparently favorable results reported by them have not as yet been corroborated by others. No further reports on the use of this preparation have appeared in the American or European literature. As the authors themselves state, more study and prolonged testing is necessary before an evaluation of the effect of this substance can be made.

TREATMENT OF SYPHILIS

To the Editor:—A woman aged 27, separated from her husband, came to me June 6, 1936, for a check up at the insistence of a partner who had contracted a virulent case of gonorrhea. She stated that she had never had a venereal infection or any symptoms relative to the genital tract and he emphatically denied any other source of contact. Another physician had previously taken urethral, vaginal and cervical smears and had found them negative. I repeated the smears and also took blood for a Hinton and a complement fixation test. The smears came back negative but the blood reports were positive for both syphilis and gonorrhea. I repeated the test and got the same results. Since then the woman has been under my care and has had the following medication with the following results: one course of neoarsphenamine totaling thirteen injections or 5.95 Gm. The Hinton test after the seventh injection gave positive results. One course of twelve thiobismol injections totaling 34.4 Gm. The Hinton test after the eighth injection was positive and the spinal fluid reading of the colloidal gold test was 00+1100000. The Wassermann reaction of the spinal fluid was negative. Because of reactions with neoarsphenamine I tried starting the second course of arsenicals with mapharsen and gave two injections of 0.04 Gm. each. On of the third injection I reverted to neoarsphenamine, giving 0.3 Gm. Twelve more injections of sulfarsphenamine were then given, totaling 3.9 Gm. The substitution was made because of difficulty with small veins. The Hinton reaction after the sixth and fifteenth treatments was still positive. After the fifteenth treatment the complement fixation test was positive. The spinal fluid examination gave a negative Wassermann reaction and colloidal gold ++-+++++000. The second bismuth course consisted of five injections of thiobismol (15 grains) and five injections of bismuth subsalicylate in oil (14 grains). There have been seven injections of sulfarsphenamine in the third course, totaling 2.1 Gm. The Hinton reaction following the last injection was still positive. To date the patient has had neoarsphenamine 6.25 Gm., sulfarsphenamine 6 Gm., mapharsen 0.08 Gm., thiobismol 49.4 grains, bismuth subsalicylate 14 grains. In conjunction she has also had two courses of yellow mercurous iodide one-eighth grain (0.008 Gm.) three times a day for one month each. She has been lax in receiving treatment and should have had nearly double this amount had she been regular. In addition she married again one year ago without permission and has since had two miscarriages at the third month. I had planned to give eight more injections of sulfarsphenamine and ten more of bismuth subsalicylate in oil before allowing a period of probation. What chance is there to develop central nervous system syphilis and what should be done to prevent it as much as possible? Is there any likelihood of infecting her husband? Will it be possible to reverse the Hinton reaction at this late date and what should be done to favor it? Would tryparsamide be indicated? Will it be possible for her to carry to term successfully?

M.D., Massachusetts.

ANSWER.—This patient has received fourteen injections of neoarsphenamine totaling 6.25 Gm., nineteen injections of sulfarsphenamine totaling 6 Gm., two injections of mapharsen totaling 80 mg., seventeen injections of thiobismol totaling 1.27 Gm. of metallic bismuth, and five injections of bismuth subsalicylate totaling 0.325 Gm. of metallic bismuth.

Some of the other data that are most necessary, however, are not furnished. No mention is made of physical examination—simply laboratory data are furnished. No mention is made of anything in the spinal fluid but the colloidal gold test and the Wassermann reaction. In an early lumbar puncture the cell count is most valuable. Moreover, it is not stated how often thiobismol injections were given. This may be one of the reasons why the patient has not responded better to therapy, though it is true that she apparently has been negligent. Studies by Sollmann, Cole and Henderson (*Am. J. Syph.* **21**:480 [Sept.] 1937) have shown that thiobismol must be administered three times a week to achieve a therapeutic lasting level of bismuth in the blood stream. If the injections are given but once a week there is little or no effect on the syphilis, for the peak level of bismuth in the blood stream after a single injection is reached and is over in twenty-four hours, and thereafter there is only a small level, which continues for a few days. On that account, if one uses thiobismol the injections must be given three times a week.

It would be well to go over the patient carefully, looking particularly for evidence of cardiovascular syphilis and for central nervous system involvement. Moreover, a lumbar puncture should be done at once, a cell count, a colloidal gold test, a Pandy test, and a Wassermann test on the fluid in amounts of 0.1 cc. up to 1 cc.

It is possible that the patient has had her syphilis for some time, and if this is true there would not be so much danger of her husband's being infected. He should be examined, however, and a Wassermann test taken.

If the lumbar puncture is done now and is negative, and the physical examination shows no evidence of central nervous system involvement, the chances are that the patient will not develop central nervous system involvement after this period of time. The Cooperative Clinical Group studies have shown that practically all involvement of the central nervous system actually occurs early in the infection although symptoms may not appear for years. Tryparsamide would not be indicated unless there is involvement of the central nervous system.

If physical examination is negative and if the lumbar puncture is entirely negative, this patient should receive alternating courses in a continuous manner of ten injections each of neoarsphenamine or mapharsen and of bismuth subsalicylate for a further period of one year and in the succeeding year two courses of injections of bismuth subsalicylate with a rest period between the courses. The Cooperative Clinical Group has already recommended that every syphilitic woman who is pregnant should be treated for syphilis throughout the pregnancy. This gives the best promise of a living, healthy child.

TULAREMIA

To the Editor:—A patient died from an infection at first presumed to have been caused by cigaret ashes which flew into his right eye. He rubbed the eye and it was red and irritated and later became infected. At first it was diagnosed as streptococcic infection but it did not respond to treatment. Blood tests were made, the first two being negative for tularemia. It had been suggested that there was a tularemic ulcer under the upper lid of the right eye. Further tests showed tularemia and treatment was given but the patient developed pneumonia and died. Autopsy disclosed the tularemia germ. As I understand it there are only about fifty cases reported of the ocular glandular type of tularemia. Could it be possible for this patient to have been bitten by a tick and for the poison to have gone through his system and settled in his eye? Is it possible for the tularemia germ to enter through the pores of the skin without the avenue of an abrasion or opening to the blood stream? A theory has been advanced that he might have smashed a tick with his fingers, wiped it on his trousers or clothes and later came in contact with it by his hands and rubbed it into his eye. The man was a fastidious individual, meticulous in his habits, and immediately preceding the episode when he got the ashes in his eye he had bathed thoroughly and had not handled any rabbits or been in contact with any. He had been out to a dude ranch the day this happened but stated that he was not bitten by a tick. Nor was he where he would come in contact with ticks other than being in the early morning outside the main ranch building with a lariat that belonged to him, throwing it to lasso a post. But after that he swam in the pool and bathed several times. His first complaint of his eye was when he and a young woman were riding home, both smoking cigarets, and a gust of wind blew the ashes into the eyes of both. The woman was not affected at all, but the patient rubbed his eye rather violently and later stopped and bathed it with water.

ROBERT R. HARROLD, North Hollywood, Calif.

ANSWER.—The presence of an ulcer from tularemia under the upper eyelid of the right eye leaves little doubt that this ulcer was the primary lesion and that the invasion of other tissues was secondary to the eye infection.

There seems to be unmistakable evidence that the causative organism of tularemia may invade unbroken skin or mucous membrane. In glandular tularemia there is no demonstrable primary ulcer. It is possible to infect guinea pigs and rabbits by dropping a suspension of infected tissue of the spleen onto the skin or into the conjunctival sac.

The development of oculoglandular tularemia usually results from inadvertently wiping the eye with fingers that have been contaminated by handling infected animals or by crushing an infected wood tick or deer fly.

ALOPECIA FROM LUPUS ERYTHEMATOSUS

To the Editor:—Since the age of 6 an unmarried woman aged 21 has had alopecia in the frontal and occipital regions of the scalp as a consequence of a probable lupus erythematosus. The few scattered hairs in the scarred regions are fine and short; the marginal hairs are longer and thicker. Hence she has had to wear a wig. What procedure besides scalp grafting is possible? Can individual hairs be sewed into the scalp? What is the relative efficacy of the different methods? Any treatment even of doubtful merit will be carefully considered. M.D., New York.

ANSWER.—Unfortunately lupus erythematosus when it affects the scalp produces areas of alopecia and atrophy. The only recourse this patient can have is wearing a wig. Grafting hair on the scalp and sewing hairs into the scalp are impossible procedures.

SYMPATHECTOMY FOR SPASTIC PARALYSIS

To the Editor:—I would appreciate information as to the merit of sympathectomy for an after-birth hemiplegic spastic paralysis due to cerebral hemorrhage. M.D., New York.

ANSWER.—The enthusiasm created by the work of Hunter and Royle during their visit to the United States in 1924, when they proposed the operation of sympathectomy for the purpose of relieving spasticity in cerebrospastic paralysis, has long since subsided. Patients who appeared to be benefited shortly after operation were found within a short time to be as spastic as they had been previous to the operation. From the standpoint of clinical experience in the use of this operative procedure, it is doubtful whether there is any permanent benefit to be derived from it.

POWDERS FOR ALCOHOLISM

To the Editor:—1. There has come to my attention recently a powder which is used to place in alcoholic beverages and causes immediate sickness; it is said to terminate the effects of overindulgence of alcohol immediately. This I cannot believe. The names of the two powders mentioned are "Micky Finn" and "Mrs. Moffat's Shoo Fly Powder." Can you give me some information on this subject? 2. Is there any powder which can be added to an alcoholic beverage that cannot be detected by taste and will cause a distaste to alcohol? M.D., Massachusetts.

ANSWER.—1. The report on the Mickey Finn Powders was sent to the American Medical Association Chemical Laboratory Nov. 22, 1918, by Dr. William D. McNally, then coroner's chemist for Cook County. The product was labeled "Mickey Finn Powders—Great Antidote for the Liquor Habit." The powder weighed from 9.57 to 13.56 grains and contained 98.19 per cent tartar emetic. Similar analysis of "Mrs. Moffat's Shoo Fly Powders" showed that each powder weighed from 2.88 to 2.97 grains. An analysis showed 98.6 per cent tartar emetic.

2. No.

POSSIBLE GLOMUS TUMOR

To the Editor:—A patient has numerous subcutaneous nodules, some about the size of a pea, some about half that size. They are painful. One of them has been removed and examined by a competent pathologist, who diagnosed it as angiofibroma. He had no treatment to offer. The patient is suffering severely and so far the only thing that I have found to give her relief has been salicylates. However, she is having as much trouble now as she had eight months ago, and I wonder whether there is any therapy that will cure this condition.

A. C. FORTNEY, M.D., Fargo, N. D.

ANSWER.—From the meager description of a painful tumor of the skin, the deduction is that this patient most probably has a glomus tumor. One might suggest a recheck of the case and comparison of the pathologic slide with the published accounts of the microscopic appearance and the clinical picture of glomus tumor. (Andrews, G. C.: Textbook of Dermatology, ed. 2, Philadelphia, W. B. Saunders Company, 1938, p. 705). Treatment consists of removing each nodule surgically. Electrosurgery also may be used.

COMPRESSES IN CELLULITIS

To the Editor:—THE JOURNAL, September 3, page 960, carries an answer to the question What is the rationale of cold compresses of magnesium sulfate in cellulitis? I would like to call your attention to the answer, which states that "hot wet dressings produce an edema of the underlying tissue and capillary changes in the vessels with a varying amount of cellular infiltration." This answer is at variance with factual information in the field of capillary physiology. Local edema due to a cellulitis does not develop if circulation is maintained. Moist heat induces local circulatory acceleration. During work muscles take up from ten to twenty times more oxygen than when at rest. Heat, within certain limits, influences oxygen diffusion about 1 per cent per degree. This indicates increased capillary circulation in order to supply the oxygen. If the circulation was not accelerated by moist heat and by functional activity, the rapid exhaustion of oxygen from the blood would result in a cyanotic color which is characteristic of poor circulation. One does not see cyanosis from the use of moist heat compresses. Carbonic acid is inseparably bound up with increased functional activity. Pure carbon dioxide will produce dilatation of arteries and capillaries and a rapid current of blood. There is no reason for believing that the accelerated circulation induced by moist heat can be produced independently of the formation of carbon dioxide. Clinically, the picture induced by muscular activity and the picture induced by moist heat are similar. Krogh (The Anatomy and Physiology of Capillaries, New Haven, Conn. Yale University Press, 1929) found when working with rabbits that if the animals were kept warm the arteries and arterioles were dilated; the capillaries were not greatly involved in the dilatation but the venules and veins were somewhat dilated by the increased flow. In the skin of man, moderate moist heat does not induce the contracted, elevated papillae of refrigeration. It must be remembered that there are no capillaries in the skin of man outside those in the papillae. In a study of capillary loops around the finger tips of man, Krogh noted that warmth allowed two corpuscles to pass the field of vision when normally only one had been noted. Under the influence of cold, agglutination of corpuscles was noted and the flow appeared retarded. Clinically, if vessels are not damaged and the circulation has not failed completely, local edema disappears under moist heat compresses. Naturally there is a limit to physiologic reactions. If capillary function has failed completely, surgery is indicated, not therapy. "Changes" in capillary walls and cellular infiltration are not the result of application of compresses of moist heat. If uncontrolled dry heat or refrigeration is used, "changes" may be expected. A better understanding of the physiology of capillary function should result in the abandonment of cold packs as a means of combating a localized suppurative cellulitis. Dental and mastoid suppurations are commonly refrigerated. The abdomen is commonly refrigerated with ice packs. Enough evidence is available today to indicate that refrigeration of a local cellulitis is empiricism.

JOSEF NOVITZKY, D.D.S., San Francisco.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, November 12, page 1871.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Medical centers having five or more candidates desiring to take the examination, Feb. 13-15. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th Street, Philadelphia.

SPECIAL BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: An Affiliate of the American Board of Surgery. Written examination, Part I, will be held in various cities of the United States and Canada, April 8. Oral examinations for all candidates, St. Louis, May 13-14. Applications must be filed not later than sixty days prior to the date of the examinations. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF INTERNAL MEDICINE: Written examinations will be held in various parts of the United States, Feb. 20. Application must be received on or before Jan. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Written examination and review of case histories of Group B applicants will be held in various cities of the United States and Canada, Feb. 4. General oral, clinical and pathological examinations for all candidates (Groups A and B) will be given in St. Louis, May 15-16. Applications must be filed not later than sixty days prior to date of examination. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: St. Louis, May 15. Applications must be filed before February 15. Sec., Dr. John Green, 3720 Washington Blvd., St. Louis.

AMERICAN BOARD OF ORTHOPÆDIC SURGERY: Memphis, Tenn., Jan. 13-14. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: St. Louis, May 12-13. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PEDIATRICS: New York, April 26. Appointments must be made before Dec. 26. St. Louis, May 16. Appointments must be made before Jan. 16. Cincinnati, Nov. 14-15. Appointments must be made before July 14. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 28-30. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: St. Louis, May 11-14. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: New York, Jan. 13-15. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

Missouri June Report

Dr. Harry F. Parker, secretary, State Board of Health of Missouri, reports the written examination held at St. Louis, June 2-4, 1938. The examination covered fifteen subjects. An average of 75 per cent was required to pass. One hundred and sixty-five candidates were examined, 162 of whom passed and three failed. Fifteen physicians were licensed by reciprocity and five physicians were licensed by endorsement July 26. The following schools were represented:

PASSED		
School	Year Grad.	Per Cent
State University of Iowa College of Medicine	(1937)	79.5
University of Kansas School of Medicine	(1933)	81.7
Johns Hopkins University School of Medicine	(1932)	85.3
Harvard University Medical School	(1937)	82.6
St. Louis University School of Medicine	(1937)	76.8, 76.8, 79, 80.4, 81.4, 81.8, 82.4, (1938) 76.9, 77.5, 78, 78.1, 78.4, 78.4, 78.9, 79, 79.4, 79.9, 80, 80, 80.1, 80.1, 80.2, 80.4, 80.5, 80.5, 80.6, 80.7, 80.8, 81.1, 81.2, 81.3, 81.4, 81.5, 81.6, 81.8, 81.8, 81.9, 82, 82, 82.1, 82.2, 82.2, 82.3, 82.4, 82.4, 82.5, 82.5, 82.7, 82.8, 83.4, 83.4, 83.8, 84.1, 84.1, 84.6, 84.7, 84.8, 84.8, 85.2, 85.2, 85.4, 85.6, 86.3, 87, 87.5, 88.4, 88.7, 89.6
Washington University School of Medicine	(1937)	75.2, 75.4, 77.7, 77.8, 81.1, (1938) 76.5, 77.2, 78, 78, 78.6, 79.2, 79.3, 79.5, 79.5, 79.6, 79.7, 79.8, 80, 80, 80, 80.1, 80.4, 80.5, 80.6, 80.6, 80.6, 80.6, 81, 81.1, 81.2, 81.3, 81.3, 81.4, 81.4, 81.4, 81.5, 81.6, 81.6, 81.6, 81.6, 81.7, 81.7, 81.8, 81.8, 82, 82.1, 82.1, 82.2, 82.2, 82.5, 82.5, 82.6, 82.6, 82.8, 82.8, 82.8, 82.9, 83, 83.1, 83.2, 83.3, 83.4, 83.6, 83.6, 83.8, 84.1, 84.1, 84.2, 84.4, 84.5, 84.6, 84.6, 84.6, 84.6, 84.8, 85, 85.2, 86, 86.4, 86.4, 87.3
Creighton University School of Medicine	(1936)	80
University of Nebraska College of Medicine	(1937)	83.1
University of Pennsylvania School of Medicine	(1937)	81.1
Baylor University College of Medicine	(1937)	85.7
University of Texas School of Medicine	(1937)	80.4
University of Wisconsin Medical School	(1937)	77.4, 78.8
McGill University Faculty of Medicine	(1923)	82.7
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin	(1937)	76.8

FAILED		
School	Year Grad.	Per Cent
School of Medicine of the Division of Biological Sciences	(1937)	74.2
Meharry Medical College	(1935) 69.6, (1937)	72.7

LICENSED BY RECIPROCITY		
School	Year Grad.	Reciprocity with
University of Arkansas School of Medicine	(1937)	Arkansas
University of Colorado School of Medicine	(1936)	Colorado
Emory University School of Medicine	(1937)	Georgia

University of Kansas School of Medicine.....(1931), (1935), (1937, 3) Kansas
University of Louisville School of Medicine..(1934), (1937) Kentucky
Tulane University of Louisiana Medical Department..(1912) Louisiana
Johns Hopkins University School of Medicine.....(1935) Maryland
Harvard University Medical School.....(1936) Maine
Creighton University School of Medicine.....(1936) Kansas
Meharry Medical College.....(1934) Tennessee

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists		(1937)	N. B. M. Ex.
Tulane University of Louisiana School of Medicine		(1936)	N. B. M. Ex.
St. Louis University School of Medicine		(1931)	N. B. M. Ex.
Washington University School of Medicine		(1936)	N. B. M. Ex.
Cornell University Medical College		(1935)	N. B. M. Ex.

Book Notices

The Biology of Arteriosclerosis. By M. C. Winternitz, M.D., R. M. Thomas, M.D., and P. M. LeCompte, M.D., the Department of Pathology, Yale University School of Medicine, New Haven, Connecticut. Cloth. Price, $4. Pp. 142, with 116 illustrations including 56 colored illustrations. Springfield, Illinois, & Baltimore: Charles C. Thomas, 1938.

This work, sumptuously illustrated in color and black and white, is a study of the results obtained by injecting suspensions of Higgins' engrossing ink into arteries and solutions of berlin blue into veins. The only variation from standard injection methods was the use of high pressures: from 800 to 1,000 mm. of mercury in the injection of coronary arteries up to 1,500 mm. of mercury in the injection of leg vessels. After injection, the tissues were cleared by the method of Spalteholz. The illustrations are for the most part drawings, with photomicrographs, some by the Kodachrome method, and photographs. There are many picturesque drawings of the various capillary and sinusoidal systems found. The authors were influenced by a hope that they could demonstrate intimal vessels in normal arteries, which previous workers had failed to do. Their work furnishes added evidence, if any were needed, that the intima of normal arteries is not vascularized, since all the illustrations of injected human arteries showing intimal vessels are the seat of advanced atherosclerosis.

Much stress is laid on the finding of hemorrhages in some atherosclerotic lesions. It is difficult to follow the reasoning of the authors that these hemorrhages may have an etiologic relation to the disease atherosclerosis. The hemorrhages arise from vessels of capillary systems that are produced to supply nutrition to atherosclerotic lesions, as these enlarge beyond the possibilities of support by diffusion through the intima. In other words, the lesions in which capillary systems are found are already advanced lesions. How hemorrhages into advanced lesions can be etiologic factors in atherosclerosis is not explained.

The possibility that infection may be the etiologic factor in atherosclerosis is again presented, despite the contrary opinion of authorities, almost without exception, who have studied this disease. The authors refer to two early papers from the University of Oregon supporting this thesis but do not refer to a later paper from the same laboratory (Menne, F. R.; Beeman, J. A. P., and Labby, D. H.: Cholesterol-Induced Arteriosclerosis in Rabbits, with Variations Due to Altered Status of Thyroid, *Arch. Path.* **24**:612 [Nov.] 1937) in which it is concluded: "In our considerations it seems evident that many agencies of disease, the variations in diet, the disturbance of internal secretions, infections, the traumatisms of certain occupations and the influence of posture all aid in the development of arteriosclerosis only as they modify these two basic factors of hypercholesteremia and mechanical strain."

The bibliography on nutrition of the blood vessel wall by Dr. Elizabeth M. Ramsey, which is republished (*Yale J. Biol. & Med.* **9**:13 [Oct.] 1936) as an appendix, is thorough. On the other hand the bibliography on arteriosclerosis lacks reference to many modern papers.

The book has value only as a study of the vascularization of advanced atherosclerotic lesions. Inferences are drawn that are not justified by the material presented and that tend to confuse the issue with respect to etiology.

The publisher is to be complimented on the makeup of the book, the reproductions and the clear type. The drawings are excellent.

Les réactions d'équilibre chez l'homme: Étude physiologique et clinique des réactions d'équilibre sur la table basculante. Par Jules Zador. Préface de M. André-Thomas. Paper. Price, 80 francs. Pp. 255, with 214 illustrations. Paris: Masson & Cie, 1938.

In this monograph Zador has attempted to extend to the clinic the experimental studies of Rademaker on equilibration, as Rademaker and Garcin had done previously. In his study he used a horizontal table on which the subject was placed in various positions, supine, prone, on the hands and knees or the elbows and knees, sitting and standing. The table was so constructed that it could be suddenly tilted, at first in only two directions about a single horizontal axis, but in a later model in four directions. The author accepts and bases his work on Rademaker's conclusions that the reactions which occur following sudden tipping of the table are labyrinthine in origin and following slow tipping are proprioceptive in origin. He is concerned only with the former and further quotes Rademaker to the effect that the reaction following sudden tipping is divisible into three phases: the labyrinthine, the passive, imposed by gravity on the body, and the proprioceptive.

He reports his observations on the normal adult in which the reaction can be simply stated as a tendency for the body to attempt to maintain the position present before the table tipped. In the infant he finds that by the age of 8 months the child attempts to maintain his position on the table but that the reaction until the age of 6 years is different and after that age is comparable to the normal adult reaction. He then records his results in a variety of pathologic conditions, disturbances of the vestibular nerves, cerebellar disease, cerebellovestibular syndrome, tabes dorsalis, hemiplegia without "static ataxia," extrapyramidal hyperkinesis, parkinsonism, catatonic stupor of dementia praecox and idiocy. In this section the book is most unsatisfactory. The clinical information is brief and often absent, and anatomic confirmation of the clinical diagnoses is wholly lacking. The reader is forced to accept the author's or his colleagues' interpretation of the cases. Such, of course, is very inconclusive and unsatisfactory in a monograph which poses as the presentation of a piece of human neurophysiologic investigation and presumes to offer a new technic for the examination and diagnosis of cases of nervous disease.

The author states that with bilateral involvement of the vestibular nerve the normal reactions are lost. They may be lost with a unilateral lesion, but compensation tends to occur and after a time the normal response may return. With chronic cerebellar disease the normal reactions are retained. Experience with acute cerebellar lesions is too limited to justify any statement and the method is not applicable to cases of tumor. With tabes dorsalis and catatonia the reactions are normal. With "extrapyramidal hyperkinesis" and in idiots the reactions revert to the infantile type. There is no index.

The Essentials of Human Embryology. By Gideon S. Dodds, Ph.D., Professor of Histology and Embryology, School of Medicine, West Virginia University, Morgantown, West Virginia. Second edition. Cloth. Price, $4. Pp. 316, with 182 illustrations. New York: John Wiley & Sons, Inc.; London: Chapman & Hall, Limited, 1938.

This is a clear and simple presentation for the use of medical students of the facts and point of view which are essential for any understanding of human anatomy. It is prefaced by an excellent discussion of the physiology of reproduction in mammals as it is understood at the present moment. The theorizing and comparisons so dear to the heart of the embryologist are reduced to a minimum. This goes too far sometimes. The human yolk sac, for example, is dismissed as a "relic." At the eight weeks stage, to be sure, it seems to be nothing more than a useless vestige, but when one considers that during the third and fourth weeks the embryo takes form as it is spread out on the surface of the yolk sac precisely as in reptiles and birds, it is obvious that the yolk sac could not have dropped out of the life history of man without fundamentally modifying the whole scheme of development. Mention is made later of it as a hematopoietic organ; up to the fifth week it is the hematopoietic organ *par excellence*. Similarly, the pronephros and mesonephros have persisted through the ages because they are essential not only for the development of the wolffian duct but for

maintaining the patency of the duct and later the urogenital sinus (Boyden). The illustrations are done in the British manner—simple line drawings free from all ambiguity. Few create false impressions. The wofully incorrect figure of the "Bulle" embryo is here as in so many other textbooks. Figure 12 gives an erroneous idea of the character and mode of spread of the implantation syncytium. The chapter on the nervous system is written from the point of view of the neurologist, which is quite unusual in works on embryology. Books of this sort are good if the instructor points out that human embryology is not as fully worked out as the text seems to indicate. He does point out that the mechanism of development is still largely a mystery, but it would have been possible to say that recent experimental studies have revealed at least some of the factors concerned in normal development.

Life, Heat, and Altitude: Physiological Effects of Hot Climates and Great Heights. By David Bruce Dill, Fatigue Laboratory, Harvard University. Cloth. Price, $2.50. Pp. 211, with 25 illustrations. Cambridge: Harvard University Press; London: Oxford University Press, 1938.

There seems no great justification for the publication of this volume. From a medical or scientific standpoint, Dill's material on the physiologic effects of high temperatures and high altitudes has already been well presented in readily available journals and its points of practical importance have been widely appreciated. Insufficient linkage exists between heat and the effects of altitude to justify his attempt at unified presentation. The chapter on desert animal life is interesting. The first sections on heat deal almost exclusively with effects on the water and salt balance and on the circulatory system, neglecting entirely the changes in internal combustion and in adrenal function that are brought about by adaptation to difficulty of heat loss. Desert animal life the author oversimplifies by division into those forms which obtain their water supply from plants and those which take it as free water. Surely there are all degrees of intervening gradation, just as exist in nondesert regions. And in his final sections on altitude effects no attention is devoted to barometric pressure as such, all observations centering around the results of oxygen deprivation. The presentation presumes to be physiologic in character, but only in the technical parts dealing with water and salt balance at high temperature and with the effects of low oxygen tensions is the material adequately handled. The medical reader will find in the book little of value that has not already been well stressed in scientific and medical journals, while for the layman the technical material and presentation make reading difficult and uninteresting.

The Occupational Treatment of Mental Illness. By John Ivison Russell, M.B., Ch.B., F.R.F.P.S., Medical Superintendent, North Riding Mental Hospital, Yorkshire, England. With foreword by William Rees-Thomas, M.D., B.S., F.R.C.P., Senior Medical Commissioner, Board of Control. Cloth. Price, $2.50. Pp. 231, with 41 illustrations by Joseph Blagdon Morgan. Baltimore: William Wood & Company, 1938.

In the foreword of this interesting book by an English physician there is a quotation from Dr. Samuel Tuke of York Retreat, written in 1841, in which he gave credit to Sir William Ellis for introducing work on a large scale to asylum patients in England well over a century ago. But to Dr. Simon of Gutersloh is given the credit, early in this country, for using work as a "soothing potion in the hands of every nurse."

The purposes and aims of occupational therapy are discussed in the introduction. These deal freely with human nature, especially as it may react to success or failure. The value of work treatment does not depend on the quality of the thing made but more on the favorable reactions of the patient. The ability to work is usually a more wholesome commentary on recovery from fatigue than almost anything else that may happen.

Under psychologic types, motives for work are discussed—among others to serve, to delight, to rule. Some handle material things, as a curator; some work with symbols, as the clerk; others tend animals, such as fanciers; some serve human beings, as nurses. Interesting case histories of various clinical reaction groups are presented to demonstrate how work has blended into the lives of patients to alloy a better compromise between health and disability. In many respects the chapter on the prescription is the most interesting. Physicians generally do not give sufficient thought to the purpose of work to formulate a satisfactory program. An ingenious form is presented enabling a prescription to be written in code form covering aims to be achieved and dangers to be avoided.

The author discusses the degree of specialization among therapists found in Germany, the Netherlands and the United States. He leads one to believe that occupational therapy should be less specialized and more a part of the regular nursing regimen. It is refreshing to know that occupational therapy embraces a great variety of work, games, hobbies, dancing, entertainments and reactional activities indoors and out, including habit training. Spontaneity is emphasized. Formalism is decried. Work for the institution is no less valuable than anything else. Whether it should be centralized or scattered depends on local conditions, but in general there should be a well recognized headquarters for work. Some chapters are devoted to special buildings and facilities, the care and selection of supplies, and the choice of designs. Short chapters devoted to individual crafts give a simple statement of essential needs.

A chapter or two correlating work therapy with psychotherapy and hydrotherapy would have added to the value of the book; also a follow-up study to ascertain what place occupational therapy holds in the retrospective memory of socially adjusted patients.

The book is well written and illustrated and has much in it that commends itself to psychiatrist, nurse and occupational therapist, whether these are separate persons or one.

Eine experimentelle Studie über Calciumoxalat als Steinbildner in den Harnwegen: Speziell mit Rücksicht auf die Bedeutung des Magnesiums. Von Greta Hammarsten. Aus dem medizinisch-chemischen Institut der Universität Lund. Paper. Pp. 155, with 40 illustrations. Lund: C. W. K. Gleerup; Leipzig: Otto Harrassowitz, 1937.

This is a monograph in which the role of calcium oxalate in relation to stone formation in the urinary tract is exhaustively studied. Many tables are presented in demonstrating the physical properties of calcium oxalate in relation to solubility. The various effects of magnesium intake and urinary magnesium excretion on the formation of calcium oxalate stones are forcefully stressed. In animal experiments using rats, stone formation was frequent when the urinary magnesium excretion was lowered with coincidental increased calcium and oxalic acid excretion. However, if vitamin A and D deficiency was added to the foregoing conditions, stone formation was still greater and damage to the renal parenchyma more marked. An acid producing diet reduced definitely the incidence of stone formation. The frequency of stone formation in a large series of animals was greater in the male, coinciding with a higher urinary calcium output in the male sex. Males showed in general a higher urinary calcium excretion. It is interesting to note that on a vitamin poor diet with very low magnesium intake the incidence of stone in the female approaches that in the male. The view that protective colloids have no demonstrable part in the prevention of stone in either sex is maintained. Experimental stones were decalcified when the diet was changed to include adequate vitamins, calcium and magnesium, provided the renal parenchyma had not been too badly damaged. The more important clinical conditions under which calcium metabolism may be disturbed, often with increased urinary calcium excretion, are (1) calcium deficiency, (2) magnesium deficiency, (3) acidosis, (4) avitaminosis A, B, C and D, (5) hypervitaminosis A and D, (6) hyperparathyroid and hyperthyroid function, (7) intestinal diseases in which the absorption of the necessary minerals and vitamins is impaired, and (8) skeletal trauma of considerable extent. Stress is laid on the fact that even with a large intake of calcium and magnesium, unless they are in a readily absorbable form, deficiency of these substances will be evident. It is erroneous to assume that calcium containing foods are to be avoided in the presence of calcium stones. If sufficient calcium in an easily absorbable form, the best of which is milk, is maintained in the diet, along with an adequate magnesium and vitamin intake, a calcium balance is maintained, keeping the excretion of calcium in the urine very low. Conversely, a paradoxical increase in calcium excretion in the urine can be maintained by too

low a calcium intake with a concomitant deficiency in fat soluble vitamin ingestion. Foods rich in oxalic acids, which are tabulated, should be avoided. A bibliography which includes more than 300 references is included in this excellent work.

A Textbook of Physiology. By William D. Zoethout, Ph.D., Professor of Physiology in the Chicago College of Dental Surgery (Loyola University). Sixth edition. Cloth. Price, $4. Pp. 714, with 291 illustrations. St. Louis: C. V. Mosby Company, 1938.

This edition of a popular intermediate textbook in physiology is in several respects an improvement on previous ones. The hormones and vitamins are more adequately treated than before. The section on higher central nervous system activity is particularly clearly written. The occasional phonetic analysis of words, as on page 170, is, however, of questionable propriety. A student sufficiently advanced to read the book should be acquainted with such words. A number of illustrations of out of date apparatus are still included, for example one of Dudgeon's sphygmograph. In general the illustrations are well selected and competently reproduced. There is a twenty page index which is well organized. A particularly distressing thing about the book is that the publisher's "blurb" on the jacket is a model for rhetorical errors and is in bad taste generally. Such statements as "In fact the entire make-up of the book was that good that it was used in schools in every state in the country with the exception of one" might easily deter one from looking seriously at the book itself.

The Living Body: A Text in Human Physiology. By Charles Herbert Best, M.A., M.D., D.Sc., Professor and Head of Department of Physiology, University of Toronto, Toronto, Canada, and Norman Burke Taylor, M.D., F.R.S., F.R.C.S., Professor of Physiology, University of Toronto, Toronto, Canada. Cloth. Price, $3.60. Pp. 563, with 283 illustrations. New York: Henry Holt & Company, 1938.

This book was written for the college student and the inquiring layman and, as far as textual material and information go, is but another textbook since it does not present any particularly new approach or any original point of view over any of those in the several textbooks now available. The information is conventionally sound and simply presented. Illustrations cover much the same ground as found in any good textbook, although many are original; others were taken from well recognized and authoritative sources, all of which are acknowledged in the preface. These critical statements need not be interpreted as derogation, for the work is unquestionably valuable, but rather as decrying the current tendency to produce more and more textbooks for which there is no real demand and which do not offer any improvement over many of those already available. Taken alone, there is nothing to criticize in this book. Taken with other current textbooks, there is nothing in particular to praise.

The Hypothalamus: Morphological, Functional, Clinical and Surgical Aspects. By W. E. Le Gros Clark, D.Sc., F.R.C.S., F.R.S., John Beattie, M.D., D.Sc., George Riddoch, M.D., F.R.C.P., and Norman M. Dott, F.R.C.S.Ed. The Henderson Trust Lectures, Nos. XIII-XVI, published for the William Ramsay Henderson Trust. Cloth. Price, 12s. 6d. Pp. 213, with illustrations. Edinburgh & London: Oliver & Boyd, 1938.

This book, which is attractively bound, is printed on excellent paper and is well illustrated and contains four lectures which comprise the Henderson Trust Lectures delivered in Edinburgh in October 1936. The lectures have been enlarged to bring down to date the knowledge concerning the morphologic, functional, clinical and surgical aspects of the hypothalamus. Every one interested in organic neurology, endocrinology and neurosurgery will find this a comprehensive review of the subject. It is written by men who are well qualified; the authors admit our limited knowledge but present clearly and concisely what is known. The anatomic relations of the hypothalamus are described and a comparison between man and lower mammals is used to emphasize similarities and differences. The lecture on the functional aspect of the hypothalamus is of clinical interest, as it is divided into sections dealing with known physiologic evidence pointing to definite functions. The lecture on the clinical aspects of hypothalamic derangement outlines the so-called 'hypothalamic syndrome,' consisting of obesity, amenorrhea, diabetes insipidus, glycosuria and disorders of sleep. The intracranial diseases which give rise to the hypothalamic syndrome are also described and discussed. Closely related to the clinical presentation is the lecture on the surgical aspect of the hypothalamus, in which cases are presented, with roentgenograms of the skull, ventriculograms, reproductions of photographs of the patients and drawings of the tumors found at operation. When the book has been read, one feels that the subject has been clearly, concisely and comprehensively presented in such a manner that every practitioner of medicine interested in the subject should consider it for his book shelf.

The Construction of Vulcanite Applicators for Applying Radium to Lesions of the Buccal Cavity, Lips, Orbit and Antrum. By Desmond Greer Walker, M.A., M.Dent.Sc., M.B., Assistant Dental Surgeon to the Royal Dental Hospital, London. Foreword by W. Warwick James, O.B.E., F.R.C.S., L.D.S. Published for the Middlesex Hospital Press. Cloth. Price, 5s. Pp. 61, with 23 plates. London: John Murray, 1938.

The treatment of malignant diseases of the mouth requires very accurate application of radiation, especially when it is applied in the form of radium therapy. Without mastery of the necessary complicated technic its imperfect use has in the past resulted in definite damage to the bone. This type of injury may now be avoided by the use of protective shields. This monograph is offered by the author as the outcome of experience gained through three years of radium work at the Middlesex Hospital in London. The employment of vulcanite applicators is carefully described, and for physicians working in radium therapy it should prove exceedingly helpful. These applicators afford a means of applying radium to sites which were previously impossible to treat, for instance the neighborhood of the anterior pillar of the fauces. The method offers a great improvement in accuracy over previous technics, and better protection for the surrounding tissues is possible by incorporating lead in the applicator.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Enucleation of Eye Resulting from Exposure to Light Incident to Electric Welding.—The claimant, in the course of his employment as a ship fitter, for several periods of from one-half hour to one hour each, Dec. 28, 1934, was exposed to the bright glare of light incident to electric welding machines. He did not wear goggles or eye protectors. He was not engaged in the operation of the machines but his work took him into their vicinity. On the day when this happened he had a "grippy" feeling but he worked all day. His eyes, he claimed, were normal except that he had to use glasses to read or draw on blueprint, but then he used only ordinary reading glasses. On previous occasions when he worked with or close to electric welding machines he had suffered some irritation of the eyes, but on this day he felt no discomfort until on his way home after work. Then his eyes "felt like some one would take a handful of sand and throw it in your eyes and cause your eyes to water all the time." When he reached home his wife sent for the family physician. She made a potato poultice to ease the irritation of the eyes. Not because of any condition of his eyes, but because he was not responding satisfactorily to the treatment for grip, a second physician, Dr. Jameson, was called in. He, however, noticed the home made remedy applied to the eyes and ordered it discontinued, suggesting the use of mild protein silver and boric acid. As the eyes got no better an eye specialist, Dr. Shemeley, was called January 4. Dr. Shemeley saw the claimant again January 7 and instructed him to go to the Wills Eye Hospital. There he was treated by Dr. O'Brien, and after several weeks of observation and treatment Dr. O'Brien enucleated the claimant's left eye.

Claiming that the loss of his eye was due to exposure in the course of his employment to the flashes of electric light caused by the electric arc welding machines, the claimant instituted proceedings under the workmen's compensation act of

New Jersey. A referee for the workmen's compensation bureau denied him compensation. The claimant thereupon appealed to the court of common pleas of Camden County, which reversed the finding of the referee and awarded compensation. The claimant's employer then appealed to the supreme court of New Jersey.

Dr. O'Brien, who had treated the claimant in Wills Eye Hospital and who had enucleated his eye, testified that the claimant had suffered from panophthalmitis, which he described as an inflammation of all the structure of the eye from "within out." In his judgment the flashes of light from the electric welding had irritated the eyes of the claimant and caused him to rub them. By rubbing them he started up virulent organisms or sources of infection, present in almost every eye, and they "broke through" the front of the eye and infected the entire organ. In Dr. O'Brien's opinion the infection did not come from within the eye or from any source back of the eye; after removing the eyeball he had examined the eye socket and found no pathologic change in its bony framework. The infection did not come from the sinuses. Dr. Shemeley, who saw the claimant only twice, January 4 and January 7, testified on behalf of the employer. Although the claimant's exposure to the flashes from the electric welding process occurred on December 28 and this witness did not see him until January 4 and although the witness admitted that it was possible for a "flash burn" to clear up in twenty-four hours, he testified that in his opinion the condition of the claimant was not due to a flash burn. In the opinion of this witness the claimant's exposure to the flashes of light from a welding machine would not have any effect on his eye.

Another medical witness on behalf of the employer, who examined the claimant April 12, some months after the eye had been removed, and who based his opinion on symptoms and conditions stated in the notes made by Dr. Shemeley on the two occasions on which he saw the claimant, was of the opinion that the infection came from within and was not the result of the exposure to the flashes of light incident to electric welding.

In summing up, the supreme court emphasized strongly the differences in the opportunities that the several expert witnesses whose testimony is referred to had had for becoming personally acquainted with the condition of the patient. Dr. Shemeley had seen the patient only twice, "on both of which instances the organ was in a very distressed condition." Dr. Dublin's testimony was predicated on an examination made a considerable time after the claimant's eye had been removed and rested in the main on charts prepared by Dr. Shemeley. Dr. O'Brien saw the claimant daily for weeks, then removed the eyeball, and thereafter kept the claimant under observation. It is not necessary, said the court, for the claimant to carry the burden of proof to the point of demonstration. It is sufficient to show that the hypothesis on which he based his claim is probable, and this, the court thought, the claimant had done. For that reason the judgment of the court of common pleas of Camden County in favor of the claimant was affirmed.—*Jackson v. New York Shipbuilding Corporation (N. J.), 197 A. 284.*

Dental Practice Acts: Suspension of License for Conviction of Crime; Subsequent Good Conduct as Mitigating Circumstance.—Brown, a licensed dentist, was convicted of manslaughter and sentenced to pay a fine and serve a jail sentence. The jury recommended clemency and he was thereafter paroled. About a year and a half later, the board of governors of the registered dentists of Oklahoma suspended Brown's license under a provision of the dental practice act authorizing the board, on presentation of a certified copy of a court record showing that a licentiate has been convicted of a crime involving moral turpitude, to revoke his license or to suspend him from practice or to reprove him. Brown appealed to the Supreme Court of Oklahoma.

The evidence showed that Dr. Brown had practiced dentistry since 1911, that he had always borne a good reputation, that he was a man of good morals and high character, that the only blemish on his record was the act which formed the basis of his conviction, and that subsequent to the conviction he bore a good reputation and maintained a high standing of character. One who has practiced his profession for twenty-three years, said the Supreme Court, maintaining at all times an excellent reputation and being in fact a man of high character, but who then is guilty of such an act of moral turpitude as was here charged against Brown, may thereafter so conduct himself by right conduct in his profession and as a citizen as to reestablish himself as a man of high character. This, in the opinion of the court, Dr. Brown had done. The board seemed to have concluded that the conviction required it to take disciplinary action without regard to the fact that subsequent to the conviction the dentist had conducted himself above reproach. That view, the court said, while doubtless entertained in good faith, was erroneous and in law constituted an abuse of discretion on the part of the board. The Supreme Court accordingly reversed the decision of the board suspending Brown's license to practice dentistry.—*Board of Governors of Registered Dentists of Oklahoma v. Brown (Okla.), 76 P. (2d) 1074.*

Society Proceedings

COMING MEETINGS

American Student Health Association, New York, Dec. 29-30. Dr. Ruth E. Boynton, Students Health Service, University of Minnesota, Minneapolis, Secretary.

Pacific Coast Society of Obstetrics and Gynecology, Los Angeles, Nov. 30-Dec. 3. Dr. T. Floyd Bell, 400 29th St., Oakland, Calif., Secretary.

Radiological Society of North America, Pittsburgh, Nov. 28-Dec. 2. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y., Secretary.

Society for the Study of Asthma and Allied Conditions, New York, Dec. 3. Dr. W. C. Spain, 116 East 53d St., New York, Secretary.

Southern Surgical Association, White Sulphur Springs, W. Va., Dec. 6-8. Dr. Alton Ochsner, 1430 Tulane Ave., New Orleans, Secretary.

Western Surgical Association, Omaha, Dec. 2-3. Dr. Albert H. Montgomery, 122 South Michigan Blvd., Chicago, Secretary.

THE AMERICAN RHEUMATISM ASSOCIATION

Fifth Annual Meeting and Seventh Conference on Rheumatic Diseases, held in San Francisco, June 13, 1938

LORING T. SWAIM, M.D., Boston, Secretary

Radiculitis Associated with Spinal Arthritis

DR. WILLIAM J. KERR, San Francisco: The radicular syndrome has been described as a symptom complex associated with hypertrophic spondylitis or osteo-arthritis of the spine. The symptoms are related to local inflammatory or degenerative processes in the spinal column adjacent to or involving the nerve roots, causing sensory and motor disturbances of radicular distribution. In some cases the autonomic nerves are affected. The symptoms are dependent on movements of the spine, relaxation of the supporting spinal structures or circumstances which cause an increase in the intraspinal pressure. Among these are the acts of coughing, sneezing or straining at stool (Dejerine's sign).

The symptoms are referable to the nerves emerging from the spinal axis. Disturbances in sensation, spasm of muscles with limitation of motion of the spine and atrophy of skeletal muscles are of common observation. These changes are evidently related to injury of the skeletal nerves. Other disturbances in the viscera and to the vessels of the trunk and extremities are related to injury of the autonomic nerves supplying these structures. Vascular symptoms in the extremities may precede swelling in the joints in some cases, suggesting that the involvement of the joint is likewise due to irritation of sympathetic nerves at the spinal axis. Any segment of the body may be affected. Those regions from which the nerves supplying the extremities emerge from the spine appear to be most frequently involved. Perhaps this is only because we are more able to recognize the patterns of symptoms related to lesions in these regions.

Altered sensations are commonly observed. Hyperesthesia or hypo-esthesia to light touch (cotton wool), to painful stimuli or heat and cold may be demonstrated by careful study of the segments involved. Pain or tenderness on pinching of the skin

may help to localize the radicular area affected. Hypertonus of the muscles in the early stages and hypotonus or atrophy in the late stages may be helpful. Any condition which increases the intraspinal pressure, e. g. pressure on the jugular veins (the Queckenstedt test) or coughing, sneezing or straining at stool, may reproduce the symptoms. This test thus is not a differential test from tumor of the spinal cord or nerve roots. The pain may be relieved by vasodilators such as amyl nitrite or glyceryl trinitrate and thus with pain simulating angina pectoris the differentiation cannot always be made by these drugs. If the symptoms are abdominal one may put the abdominal muscles on tension, and tenderness on palpation will disappear, whereas in peritonitis the tenderness will persist.

The segmental areas involved will generally direct attention to the segments of the vertebral column which are involved. Local tenderness of the spine, pain on motion and stiffness of the spinal column may be found if the process is active or recent, or rigidity may exist without other signs if the process is quiescent. Films of the spine may show few changes early when symptoms are acute but generally there is some evidence of changes in shape or density of the bodies of the vertebrae or intervertebral disks, some fuzziness or narrowing of the foramina, or spurring of the margins of the vertebrae or the articular facets with the ribs. Changes in the spinal curves and scoliosis may be shown best by films. In some cases marked osteo-arthritic changes are shown by x-ray examination when there are no symptoms. Almost invariably there are detectable signs and the patient has forgotten the acute manifestations.

The treatment is effective in many cases. In patients whose occupations place undue strain on certain parts of the spine, some relief may be obtained by changing to another occupation which puts less strain on the spine. The most frequent contributing factor is distortion of the spinal column by excessive weight on the trunk. The pendulous abdomen accentuates every curve. The lower lumbar and lumbosarcal and sacro-iliac joints suffer most but compensatory changes in the upper thoracic and cervical spine usually give symptoms in the upper extremity or in the upper cervical region, with frequent radicular symptoms in the occipital region. Abdominal support and dietary management frequently relieve the symptoms in this group.

Temporary symptomatic relief may be obtained from drugs (salicylates) or from local heat, which may be moist heat, radiant heat, electric pad or the use of a hot electric iron or flat iron moved back and forth along the spine over several thicknesses of a bath towel. Gentle massage and manipulation may be helpful. In some cases of cervical arthritis, stretching of the neck may be resorted to with great relief. Other more radical measures are generally unnecessary. Violent manipulations have been known to cause fractures of the vertebrae or their processes and therefore those who practice spinal adjustments should be avoided. The orthopedists are learning to treat these patients more rationally and often with great benefit, but other specialists in the surgical field have much to learn about the diagnostic features of the syndrome. The abdominal scars, often multiple, seen on many of these patients bear testimony to hasty judgment in the interpretation of symptoms.

Nonrheumatic "Growing Pains" and Subacute Rheumatic Fever

DR. M. J. SHAPIRO, Minneapolis: Painful extremities in children have been given a variety of names, such as growing pains, muscular rheumatism and muscle and joint pains. In a number of recent articles from 8 to 50 per cent of children considered as rheumatic have been so diagnosed on the basis of pain in the extremities alone. Actually, an analysis of the histories of 100 of the patients with well developed rheumatic heart disease at the Lymanhurst Health Center reveals that 84 per cent of them gave a definite history of a major attack of rheumatic infection: either rheumatic fever or chorea, or both. A critical study of the remaining 16 per cent demonstrates that in practically every instance, in spite of the fact that no history of a major attack of rheumatic infection was obtained, there was definite evidence that they were suffering from a long continued rheumatic infection. They presented the well known signs and symptoms of chronic rheumatic infection, such as low grade fever, loss of weight, definite joint pains, nosebleeds, skin rash, increased sedimentation rate and pallor, although their symptoms were not severe enough to put them to bed.

A follow-up study on 200 children who complain only of leg pains has been carried out at the Lymanhurst Heart Clinic for the past three years. None of them have presented any evidence of chronic rheumatic infection. They complain of pain primarily in the lower extremities. The pain comes on commonly at the end of the day and often awakens the patient during the night. They rarely complain of pain during the day and practically never have symptoms in the upper extremities. They are usually in good health otherwise, and none of them have developed rheumatic heart disease. Laboratory studies of these patients give normal results. This syndrome is so common in healthy school children during early childhood and adolescence that it is suggested that their complaint is due to normal growth. It is clear that they are not suffering from rheumatic fever and should not be so considered.

Many children with growing pains alone have been subjected to tonsillectomy, sinus drainage, periods of rest in bed, vaccine treatment, and so on on the erroneous conception that they were suffering from rheumatic fever. It would appear that the old idea that normal growing children do suffer from growing pains is probably correct. Much of the confusion could be avoided if the term "growing pains" was not used in connection with rheumatic fever.

DISCUSSION

DR. T. DUCKETT JONES, Boston: This report should do much to clear up the vagueness which exists concerning the joint manifestations of rheumatic fever. Especially harmful has been the attempt to label a child as prerheumatic with little or no justification. The absence of a specific diagnostic test is the cause of the difficulty. The development of heart disease of the rheumatic type is the most definite existing proof that a child has had rheumatic fever. In my experience, definite arthralgia has occurred at some period of active rheumatic fever in fully 70 per cent of a large series. The type of pain has been well described by Dr. Shapiro. Joint symptomatology may be real, but it is rarely of a chronic nature, and other features are much more significant. I should heartily agree with Dr. Shapiro that so-called growing pains in a child, without a frank history of previous rheumatic fever, do not frequently occur with other manifestations of rheumatic fever or a tendency to develop subsequent rheumatic heart disease. This has proved to be true even in families in which there are one or more definite rheumatic fever subjects. It is common today to see definite rheumatic fever with the development of rheumatic heart disease, without joint symptomatology, at the time of acute illness. Abundant clinical and laboratory evidence supports this view. In the carefully followed rheumatic child, mild to severe acute illness is almost invariable, and vague syndromes rarely exist. The insidious or asymptomatic development of rheumatic heart disease in children is uncommon, but in the young adult it is observed. This demonstrates that silent rheumatic fever does exist, but in following such a group I have been impressed with the frequency with which abnormal laboratory data are found either by electrocardiogram or by such nonspecific measures as the white blood count or sedimentation rate. Dr. Shapiro has noted that these tests are normal in children with growing pains, and this would seem significant to me. I should like to ask Dr. Shapiro whether he has followed any appreciable number of children with vague muscle aches and pains for a significant period of time? Dr. Shapiro's differentiation is not only important to the problem of the individual child but should help us in the broader aspects of the problems of rheumatic fever. Especially, it should help prevent the partial invalidism and even institutional care of a large group of children so often mistakenly thought to have rheumatic fever.

DR. J. ALBERT KEY, St. Louis: I am glad that the growing pains are coming back again. I have told the parent "this child has growing pains" and had them reply "I am sorry, but my doctor tells me that growing pains are old fashioned and they don't have them any more." As a matter of fact, people do have growing pains. Most growing pains, I think, are not to be classed as epiphysitis but as epiphysial strains. It is also conceivable, as Dr. Hitchcock just suggested to me, that growing pains are due to a strain of muscles: bones may grow faster

than muscles and fascia and cause strains at the muscular attachments. A third explanation is that they may be due to actual stretching of the nerves due to rapid growth of bones.

DR. M. HENRY DAWSON, New York: Could it be found whether an actual quantitative study has been done on growth during that period in which growing pains occur? Do the pains occur most frequently in individuals who grow most rapidly?

DR. FRANKLIN R. NUZUM, Santa Barbara, Calif.: As an index of how prevalent the belief is that growing pains in children do mean rheumatic fever, I reviewed six current medical textbooks and found that three of them stress the importance in the history of the occurrence of so-called growing pains in arriving at a diagnosis of rheumatic fever. Dr. Shapiro, on the other hand, has shown that among his own patients this type of pain occurs in healthy growing children. He has further substantiated his argument by following for a period of years a group of children that were referred to him with a diagnosis of rheumatic fever and whose chief complaints were "growing pains." He found that other symptoms of rheumatic infection did not develop: laboratory tests were negative, their symptoms continued to or through adolescence and disappeared, and further repeated examinations after a period of years demonstrated that rheumatic heart disease had not developed in any of this group. The latter is a most convincing point, since approximately 75 per cent of children with rheumatic infection do develop clinical evidence of heart disease. Just as it is incorrect to attach the stigma of rheumatic fever to a child who complains of muscle pains occurring especially at night, so is it incorrect to give the name rheumatic fever to the secondary arthritides that may complicate scarlet fever, pyemia, cerebrospinal fever, dysentery and other acute infectious diseases. When a single articulation is affected in a child, the condition rarely is due to rheumatic fever. The same is true of the disorder of more than one joint that remains stationary for many days, especially in the first attack. The intervertebral articulations are seldom involved in rheumatic fever but often are involved in tuberculosis and gonorrheal infections. It is generally believed that every child who has rheumatic fever suffers some damage to the heart. In about 75 per cent the degree of inflammation is sufficient to result in evident damage to the valve leaflets, the heart muscle or both. In those instances in which physical examination does not elicit evidence of heart damage, an electrocardiogram may be used as an aid in making the differentiation between rheumatic fever and recurring muscular pains of other etiology. In the former, abnormal curves are obtained in about 90 per cent; in the latter, normal curves are usually found. The abnormal electrocardiograms present a variety of changes; among them, a delay of conduction time between auricle and ventricle, abnormalities of the P or auricular wave, and/or of the RS-T or ventricular segment. The importance of an accurate history as an aid in arriving at a diagnosis of rheumatic fever bears emphasis. Dr. Shapiro has implied that this part of the study should not be detailed to a nurse assistant or an intern but should be carried out by the physician himself.

DR. M. J. SHAPIRO, Minneapolis: I have consulted a number of investigators interested in the study of growth and have tried to get an opinion on this subject. They all agree that normal growth might possibly produce such symptoms but they would not commit themselves. I have made no claim that this clinical entity is due to growth. I suspect that it is, because it is so common. Those of us who have been working on the subject of rheumatic fever are, I believe, responsible for most of the errors that are made. We have carried on propaganda for many years to impress the public with the idea that there was no such thing as "growing pains," that growth was painless, and that "growing pains" in most instances were manifestations of rheumatic fever. As Dr. Key has stated, many children with "growing pains" are referred to private physicians and clinics with a previous diagnosis of rheumatic fever. In answer to Dr. Jones's question as to how long these patients had been followed, I may state that this study was set up three years ago. All patients with "growing pains" who in my opinion were not suffering from rheumatic fever have been included in this group. The clinical picture is so similar that statistical study seems hardly necessary although it is admitted that these patients have not been followed long enough. Up to the present time, none of them have developed rheumatic heart disease. As Dr. Dawson has pointed out, it will be of considerable interest to determine whether or not these children have most of their symptoms during the period of most active growth. Such a study is now being carried out.

Metabolic Factors in the Induction of Carditis

DR. MARK P. SCHULTZ, Washington, D. C.: Nonpurulent carditis was induced in rabbits and guinea pigs subject to chronic focal, hemolytic streptococcus infection while being treated with moderate doses of thyroid; suitable controls were negative. When dinitrophenol was substituted for thyroid under similar conditions, no cardiac lesions resulted. In guinea pigs affected with chronic focal infection while receiving maximum tolerated doses of insulin, valvular and myocardial lesions developed similar to those observed in infected, scorbutic animals: the association here of scurvy as a complicating factor was improbable. An attempt was made to determine which of several attributes of the scorbutic state are factors in the development of nonpurulent carditis during the course of associated focal infection; viz., acidosis, adrenal damage or increased metabolic rate. The hearts of guinea pigs with chronic focal infection forcibly fed large doses of acidic salts were negative. No cardiac lesions were observed in adrenalectomized rats with chronic focal infections. The nonpurulent carditis observed in infected guinea pigs with chronic scurvy was of greatly increased incidence and severity in such animals treated concurrently with ultraviolet irradiation to enhance further their metabolic rate above that degree of elevation associated with uncomplicated scurvy. The increased metabolic rate in scurvy is probably a factor in the induction of nonpurulent carditis during the course of infection.

These experiments demonstrated that the induction of various metabolic anomalies in experimental animals during the course of chronic focal infection conduces to the development of nonpurulent carditis. In this connection the possible significance was suggested of the relatively frequent development of rheumatic fever and exophthalmic goiter in the same individuals and the cessation of rheumatic fever activity in those patients developing diabetes.

DISCUSSION

DR. K. K. SHERWOOD, Seattle: These experiments show that part of the result is due to the metabolic state of the animal at the time of the experiment. I should like to ask the author whether he subscribes to the view that this increased metabolic rate automatically increases the vitamin C requirement. In relating these experiments to the clinical problem, the question arises as to the absorption of the available dietary vitamin C. We know that human beings with atrophic arthritis and rheumatic fever frequently require an extremely high vitamin C intake for a long time before it becomes reflected in the blood level. The third question concerns edema in low vitamin C states. It seems to me that part of the therapeutic effectiveness of vitamin C lies in a partial control of edema in certain rheumatic states.

DR. JAMES F. RINEHART, San Francisco: The interpretation of Dr. Schultz's experiments is not easy. The production of a carditis in rabbits and guinea pigs treated with thyroxine or thyroid substance and subjected to streptococcic infection is probably explainable on the basis of an induced vitamin C deficiency incident to the action of the thyroid substance. Schuelter found that thyroid depleted the organ content of vitamin C while dinitrophenol did not have this effect. If the augmentation of the nonpurulent carditis of scurvy and infection by irradiation induces a hyperthyroid state with the increased activity of the heart, one would expect an augmentation of the carditis. The possibility of irradiation introducing another toxic influence must be borne in mind. The experiments with insulin are more difficult to interpret. However, it would appear pertinent to investigate the effect of prolonged large doses of insulin on the vitamin C metabolism. I believe the induced cardiac pathologic conditions in this series of experiments was less striking than in the thyroid experiment and I am not agreed that they resemble those of rheumatic fever as closely as those of scurvy and infection. In my experience significant cardiac lesions resulted only from the combined influence of infection (chiefly of the hemolytic streptococcus type) and vitamin C deficiency and rarely if at all in uncomplicated vitamin C

deficiency. The experimental production of a carditis and arthritis and the occasional development of subcutaneous nodules affords an unusually broad experimental basis for the thesis that vitamin C deficiency enters in the etiologic mechanism of rheumatic faver. Metabolic studies indicate that depletion of vitamin C is the rule in rheumatic fever. The concept that vitamin C deficiency contributes to the etiology of rheumatic fever has as yet been inadequately investigated in the clinic. Well controlled and prolonged therapeutic and prophylactic experiments remain to be done and to me appear clearly indicated.

DR. J. ALBERT KEY, St. Louis: Since it is conceded that with infection there is an increased demand for vitamin C, it is possible that here the infection may be the primary factor. It also appears to me that possibly the thyroid which was given acted as a direct toxin on the heart and that the reason these animals developed carditis was that their heart was damaged and the organisms attacked the point of lowered resistance. It is also important to know what other lesions these animals had in addition to their carditis. It may be that these experiments reduced their general resistance much as Pasteur did when he had his chickens stand in cold water. Finally it should be pointed out, as Kinsella noted last year before the Association of Physicians, that the primary lesion in rheumatic fever is not a purulent lesion. There is considerable difference between the primary lesions in rheumatic fever and the primary lesion induced by any known streptococcus. In a streptococcic infection the primary cell reaction is a polymorphonuclear leukocyte infiltration in the damaged area and, as I understand it, in rheumatic fever this does not occur. I don't think that we have the right to correlate a late fibroma induced by any means whatever with rheumatic fever because it resembles a late rheumatic lesion.

DR. T. DUCKETT JONES, Boston: Dr. Schultz's work has been presented in a straightforward manner, and no involved claims concerning etiology were made. A most salutary phase of the work is that it carries to the laboratory some of the features observed in patients with the disease in question. It should stimulate further attempts to reproduce rheumatic fever experimentally by means of variations and features observed at the bedside. There has been a tremendous amount of experimental work with streptococci in the past forty years, without any proof that any form of streptococcus is the cause of rheumatic fever. This should not only make us critical of any new theories but spur us on to renewed effort along lines at variance with ordinary accepted ideas. It is pertinent to mention the work of Dr. Rinehart and his co-workers on the possible role of vitamin C in rheumatic fever. In our experimental studies with guinea pigs the same lesions were found in animals with acute scurvy as in those with chronic scurvy and superimposed streptococcic infection. It has seemed to us that the streptococcic infection produced a complete scorbutus and that this was responsible for the lesions in the guinea pig heart. Dr. Schultz has told me that he has been unable to confirm this observation and suggests as a reason the frequent finding of an unsuspected streptococcic infection in guinea pigs kept in the laboratory. This is a possibility, but more important would seem to be the distinct variations in diet used. It may be well to add a further word of caution concerning vitamin C, since it has been mentioned freely and may well be important in rheumatic fever. My remarks concern the obvious pitfalls in considering such features as the geographic distribution and seasonal incidence of rheumatic fever as furthering any particular etiologic hypothesis. The geographic incidence of rheumatic fever is unknown. We speak glibly of its absence in the South, and yet every intelligent survey in areas where the disease is thought to be nonexistent indicates the fact that the disease is present, though it may be uncommon. Just recently in southern Florida I have seen a number of natives with definite rheumatic fever. In this area fruit is cheap and sunshine abundant. Also hemolytic streptococcus infections in this area are uncommon. We have streptococcus immune body studies on a group in this community, and although respiratory infection is common, specific hemolytic streptococcus immune bodies rarely develop. It is not entirely reasonable, therefore, to consider the availability of inexpensive vitamin C and the geographic distribution of rheumatic fever as necessarily being important from an etiologic point of view.

DR. DAVID FERGUSON, Bremerton, Wash.: Dr. Key brought up an important point in asking whether the pathologic condition found in the hearts of the animals that had thyroxine was not due to thyroxine rather than to infection. McEachern and his associates have definitely shown that focal necrosis as the pathologic lesion in thyroid heart disease does not occur. In fact, no anatomic changes occur in the heart as the result of hyperthyroidism. Dr. Schultz seems to show that there is some curious synergistic effect resulting from the combination of infection and thyroxine.

DR. MARK P. SCHULTZ, Washington, D. C.: I wish to emphasize the comment of Dr. Jones that the experimental lesions which have been described are not presented as those of rheumatic fever, although in my opinion they do somewhat resemble them. Concerning such experimentally induced lesions the conception is, of course, offered that the human disease is actually reproduced and that the failure to duplicate it actually is due to species differences in reactivity. It is doubtful that on the basis of the evidence at present available such a conclusion may be reached with respect to the observations which have just been presented. Dr. Sherwood has pointed out that coincident with an increased metabolic rate the vitamin C requirements of the organism are increased and that consequently the pathologic changes which were induced may have been occasioned by concomitant scurvy. In rabbits treated with thyroxine the validity of such a conclusion seems improbable, as this species belongs to the group not susceptible to such nutritional deficiency. The guinea pigs treated with insulin, it should be emphasized, received sufficient ascorbic acid subcutaneously to protect them in event of a complete absence of this vitamin from other sources against all the manifestations of scurvy except the microscopic tooth changes. In addition, because their appetites were inordinately increased and cabbage was liberally supplied in measured quantities, they are known to have consumed from eight to ten times the amount of vitamin C which has been found adequate to protect such animals against scurvy when no other source of the vitamin is present. The same is true of the rabbits and guinea pigs treated with thyroxine or desiccated thyroid gland. Dr. Heninger and others have recalled the fact that cardiac lesions resembling some of those which have been described here have been reported induced in experimental animals merely by treatment with thyroid and suggest that the results which have just been outlined were possibly due to an uncomplicated toxic effect of thyroid. I feel that this is unlikely for two reasons: First, a detailed study of the literature bearing on this point brings to light the fact that in most papers reporting the induction of damage to the heart through action of an excess of thyroid alone it is also reported, without particular significance being attributed to the circumstance, that accidental infection was present in the animals under observation. In studies such as those of Rake and McEachern, in which the presence of infection is rightly excluded during the period of thyroid treatment, no cardiac damage is observed. Second, the hearts of our control animals which received thyroid but were not infected were essentially normal. Dr. Jones and his colleagues and others have recently reported the development of cardiac lesions in guinea pigs of the type originally described by Dr. Rinehart and his associates, and of that under discussion here, in animals subject to scurvy not complicated by infection. My experience has been to the contrary, for the hearts of guinea pigs dying from the effects of scurvy have been essentially normal in those instances in which the presence of infection could be excluded with certainty. The wide prevalence of spontaneous hemolytic streptococcus lymphadenitis in guinea pig stock is probably responsible for the difficulty on this point. It has been my experience that positive cultures may be obtained from subcutaneous areas in the cervical, inguinal and axillary regions in many instances in which cultures of the blood and various internal organs are negative. Unless cultures are made from the parts mentioned it is improbable that the presence of infection can be excluded without question.

(To be continued)

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

8: 133-164 (Oct.) 1938

Optimistic View of the Problems of Heart Disease. T. M. McMillan, Philadelphia.—p. 133.
Present Status of Treatment of Pneumonias. O. W. Bethea, New Orleans.—p. 140.
Infant Mortality. W. G. Casey, Talladega.—p. 144.
Irritable Colon. I. C. Berrey, Birmingham.—p. 146.
Treatment of Lobar Pneumonia. L. C. Davis, Gordo.—p. 150.

American J. Digestive Diseases, Huntington, Ind.

5: 461-548 (Oct.) 1938

Carbonate Excretion in Urine as Indication of Alkalosis. L. C. Gatewood, Chicago.—p. 461.
Variations in Enzymatic Activity of Duodenal Contents: Preliminary Report. V. C. Myers, A. H. Free and A. J. Beams, Cleveland.—p. 464.
Triple Mechanism of Chemical Phase of Gastric Secretion. B. P. Babkin, Montreal.—p. 467.
Present Status of Treatment in Chronic Gastritis: Gastroscopic Observations. W. A. Swalm and L. M. Morrison, Philadelphia.—p. 472.
Psychiatric Contributions to Study of Gastrointestinal System. E. D. Bond, Philadelphia.—p. 482.
*Studies on Use of Aluminum Hydroxide Gel in Treatment of Peptic Ulcer. E. S. Emery Jr. and R. B. Rutherford, Boston.—p. 486.
*Level of Ascorbic Acid in Blood and Urine of Patients with Peptic Ulcer. D. T. Chamberlin and H. J. Perkin, Boston.—p. 493.
Vagotomy Plus Partial Gastrectomy for Duodenal Ulcer. A. Winkelstein and A. A. Berg, New York.—p. 497.
Development and Healing of Gastric Ulcer: Clinical, Gastroscopic and Roentgenologic Study. W. L. Palmer, R. Schindler and F. E. Templeton, Chicago.—p. 501.

Aluminum Hydroxide Gel in Peptic Ulcer.—Emery and Rutherford used colloidal aluminum hydroxide in the treatment of eight cases of the severe type and four of the moderately severe type of peptic ulcer. Five of the patients were treated by the drip method and seven by the oral method. Those patients who started on the drip method were shifted to the oral method after one week. A solution of one part of the aluminum hydroxide (creamalin) to three parts of water was used at all times. The amount which was used varied slightly, but on the average 15 drops per minute was allowed to drip through the tube. It was given orally in amounts of 60 cc. of the mixture per dose. A dose was given every hour from 8 a. m. to 9 p. m. In addition to the aluminum hydroxide, the patients were fed according to the schedule outlined by Sippy. All patients were relieved of pain due to the ulcer within twenty-four hours and had no recurrence of pain while remaining on the treatment. Colloidal aluminum hydroxide in addition to neutralizing the secreted acid decreases the titratable acidity of the gastric juice. Oral administration of the drug produces a somewhat slower decrease in the titratable acidity, which ultimately reaches the same general level. All patients who fail to respond satisfactorily to the Sippy regimen should be treated with aluminum hydroxide before surgical intervention is carried out. Colloidal aluminum hydroxide is also useful for treating ulcer patients who show a tendency to form renal calculi. The drug is absorbed but slightly and does not interfere with the acid base balance. It proved to be useful in treating four patients who had nephrolithiasis.

Ascorbic Acid and Peptic Ulcer.—Chamberlin and Perkin estimated the ascorbic acid in the blood of twenty-seven hospitalized patients with peptic ulcer. Lower levels of ascorbic acid were found in the blood and urine of these patients than in normal individuals or patients with functional digestive disorders. That patients with peptic ulcer require a greater amount of ascorbic acid is demonstrated by the fact that daily medication with ascorbic acid results in an earlier and greater excretion of ascorbic acid in the urine of normal individuals and patients on other dietary management than in patients with peptic ulcer. The amount of additional ascorbic acid required to raise the excretion of ascorbic acid to normal in patients with peptic ulcer appears to be 50 mg. four times a day. It is suggested that the metabolism of ascorbic acid is influenced by activity and that lower blood and urine values are found in patients resting in bed than in active persons.

American Journal of Diseases of Children, Chicago

56: 723-956 (Oct.) 1938

Reactions Following the Use of Diphtheri Toxoid: Analysis of Reactions and of Guides to Their Occurrence. C. R. Hayman, New York.—p. 723.
Effect of Vitamin B_1 on Iron Retention of Normal Infant. F. W. Schlutz, Helen Oldham and Minerva Morse, Chicago.—p. 735.
*Cervical Rib in Early Life. D. B. Davis, New York, and J. C. King, Memphis, Tenn.—p. 744.
Permeability of Blood Sulfocyanate Barrier to Sodium Bromide in Experimental Poliomyelitis. E. H. Lennette and D. H. Campbell, Chicago.—p. 756.
Lead Poisoning: Report of Case, with Some Physicochemical Considerations. I. Kowaloff, Brooklyn.—p. 764.
Making a Corrective Shoe. L. Bivings, Atlanta, Ga.—p. 775.
*Acute Bulbar Poliomyelitis Following Recent Tonsillectomy and Adenoidectomy. M. Stillerman, Great Neck, N. Y., and A. E. Fischer, New York.—p. 778.
Copper and Iron in Human Blood: Comparison of Maternal and Fetal Blood After Normal Delivery and After Cesarean Section. A. Sachs, V. E. Levine, W. O. Griffith and C. H. Hansen, Omaha.—p. 787.
Human Passive Transfer Antibody: IV. Studies on Children Hypersensitive to Foods. V. W. Lippard and W. M. Schmidt, New York.—p. 797.
Effect of a Milk Supplement on the Physical Status of Institutional Children: III. Progress of Dental Caries. Lydia J. Roberts, Stella Englebrecht, Ruth Blair, W. Williams and Marguerite Scott, Chicago.—p. 805.
Bronchiectasis in Children, with Special Reference to Prevention and Early Diagnosis. Antoinette Raia, New York.—p. 852.

Cervical Rib in Early Life.—Davis and King state that in the latter half of 1936 three children with cervical rib were seen at the John Gaston Hospital and at the outpatient clinic. This succession of cases suggested that similar cases might previously have been overlooked. Therefore 1,000 consecutive roentgenograms of the chests of children less than 13 years of age were studied. The incidence of cervical rib in the 1,000 consecutive roentgenograms was 1.2 per cent. Reproductions of the roentgenograms in the twelve cases are depicted. Ten of the cases were bilateral and the two unilateral ones were affected on the left. Only two were in male children. Every patient with cervical rib had a long neck and a hyposthenic thorax. A marked variation was noted in the size and contour of the anterior root of the transverse process of the seventh cervical vertebra. In many instances it reached such proportions that it was difficult to differentiate it from a rudimentary cervical rib. This may be explained by the developmental anatomy of the seventh cervical vertebra. The diagnosis of cervical rib will be made more frequently if the symptom complex is borne in mind. Oblique roentgenograms of the neck and the upper part of the chest taken with the rays directed upward, laterally and posteriorly through the seventh cervical vertebra will demonstrate more clearly the actual proportions of the rib. In the interpretation of roentgenograms of children less than 5 years of age, the presence of a separate piece of bone adjacent to the transverse process of the seventh cervical vertebra should be recognized as a center of ossification which is a potential precursor of a cervical rib.

Poliomyelitis Following Tonsillectomy.—Stillerman and Fischer studied the 686 patients with poliomyelitis who were admitted to the Willard Parker Hospital during 1935 in order to determine whether the removal of the tonsils and adenoids in any way influenced the onset or clinical type of the disease. It was found that tonsillectomy and adenoidectomy had been performed in ten cases during the month antedating the illness. In eight of these poliomyelitis began from ten to twelve days and in the other two sixteen and twenty-two days, respectively, after the operation. Six of the ten patients had the bulbar or encephalitic form of the disease. Careful inquiry

was made among the fifty-two patients with poliomyelitis that were admitted to the hospital during 1937. In three of these patients tonsillectomy had been performed from two to three weeks preceding the onset of poliomyelitis. These three children had the bulbar type of disease. All of them died. The bulbar or encephalitic type of poliomyelitis was present in sixty-eight of the 686 patients and in fifteen of the fifty-two patients, while in six and three patients respectively who recently had their tonsils and adenoids removed the bulbar or encephalitic type developed. Thus there was a disproportionately high percentage of bulbar involvement in the tonsillectomized patients in both the 1935 and the 1937 outbreak. This much higher incidence of bulbo-encephalitic forms suggests the operative field as the port of entry of the virus. They conclude, therefore, that tonsillectomy and adenoidectomy should not be encouraged during an epidemic of poliomyelitis.

Archives of Dermatology and Syphilology, Chicago

38: 511-678 (Oct.) 1938

Contact and Environmental Allergens as Cause of Eczema in Infants and in Children. E. D. Osborne and H. L. Walker, Buffalo.—p. 511.
Mycologic Technic for Study of Anascosporous Yeastlike Fungi. D. A. Berberian, Beirut, Syria.—p. 526.
*Liquefying Nodular Panniculitis: Report of Case. B. Shaffer, Philadelphia.—p. 535.
Parapsoriasis en Plaques Disséminées and Incipient Mycosis Fungoides: Supplementary Data on Their Relationship. H. Keil, New York.—p. 545.
Juvenile Pemphigus: Effects of Germanin in Three Cases. C. C. Tomlinson, with collaboration of O. J. Cameron, Omaha.—p. 555.
Is Lichen Nitidus a Variety of Lichen Planus? F. A. Ellis, Baltimore, and W. F. Hill, Philadelphia.—p. 569.
Melanotic Sarcoma with Extreme Melanosis: Report of Case. H. A. Dixon, Toronto.—p. 574.
Psoriasis of Nails. G. M. Crawford, Boston.—p. 583.
Serologic Paradox in Juvenile Dementia Paralytica: Report of Case. S. M. Bouton Jr., Ingleside, Neb.—p. 595.
*Treatment of Herpes Simplex with Moccasin Venom. R. J. Kelly, New York.—p. 599.
Multinucleated (Giant) Cell Tumor of Gum (Epulis). W. Sachs, Jersey City, N. J., and W. Garbe, Toronto.—p. 603.
Zosteriform Lichen Planus. M. I. Davis, Nashville, Tenn.—p. 615.

Liquefying Nodular Panniculitis.—Shaffer presents a case of nodules in the subcutaneous fatty tissue, associated with fever. The essential clinical features are that (1) deep-seated, painful and tender, woody nodules appeared in the subcutaneous fatty tissue, (2) they evolved in from seven to ten days into cystic masses containing from 1 to 4 ounces (30 to 120 cc.) of an oily or fatty yellowish brown fluid, (3) just before rupture (from ten to fourteen days) the skin overlying the mass was livid and raised while the central portion was attenuated into a thin translucent bulla-like membrane, (4) a deep cuplike depression formed in the subcutaneous fat, associated with a thin puckered scar, at the site of the healed lesion, (5) fever was present when the active lesions were most numerous and (6) the lesions occurred on the buttocks and extremities. The histologic features of the process are a primary round cell infiltration, the disappearance of the fat cells and their replacement by foam cells and the eventual liquefaction of the process.

Treatment of Herpes Simplex with Moccasin Venom.—Kelly treated fifteen cases of herpes simplex and three of herpes zoster with moccasin venom in a 1:3,000 dilution. The venom was given intradermally in doses of 0.2 cc. Since the disease is usually of short duration, an attempt was made to treat it only in the incipient stage, i. e. when itching, burning, swelling and slight vesiculation were present. In twelve cases of herpes simplex in which treatment was begun early, i. e. within eight to twenty-four hours after onset, the subjective symptoms disappeared within five to twelve hours after the snake venom was injected and the swelling and vesiculation disappeared within twelve to thirty-six hours, the vesicles being replaced by small dry crusts with no exudation. In the three other cases, in which the eruption had been present for longer than twenty-four hours, the duration and course of the disease were unaltered, although the patients stated that the subjective symptoms were noticeably lessened. The course of the disease in the three cases of herpes zoster appeared to be unaltered. However, the patients, each of whom had complained of severe burning and itching when first seen during the stage of vesiculation, stated that the subjective symptoms were alleviated.

Iowa State Medical Society Journal, Des Moines

28: 473-524 (Oct.) 1938

General Indications and Contraindications for Operative Delivery. E. D. Plass, Iowa City.—p. 473.
General Consideration of Occipitoposterior Positions During Labor. L. E. Kelley, Des Moines.—p. 475.
The Forceps Operation. H. A. Weis, Davenport.—p. 476.
The Aftercoming Head. W. F. Mengert, Iowa City.—p. 478.
The Cesarean Problem. E. D. Plass, Iowa City.—p. 481.
Other Obstetric Operations. O. N. Glesne, Fort Dodge.—p. 483.
Maternal Hazards of Operative Delivery. J. H. Randall, Iowa City.—p. 485.
Hazards to the Fetus in Operative Deliveries. R. E. Crowder, Sioux City.—p. 487.

Journal of Nutrition, Philadelphia

16: 309-406 (Oct.) 1938

Production of Manganese Rickets in Rats. H. Blumberg, D. H. Shelling and Deborah A. Jackson, Baltimore.—p. 317.
Spectrum Analysis for Trace Elements in Ashes of Human, Goat and Cow Milk. W. F. Drea, Colorado Springs, Colo.—p. 325.
Excretion of Vitamin B_1 in Urine and Feces. R. F. Light, A. S. Schultz, L. Atkin and L. J. Cracas, New York.—p. 333.
Study of Biophotometer as Means of Measuring Vitamin A Status of Human Adults. L. E. Booher and D. E. Williams, Washington, D. C.—p. 343.
Nicotinic Acid in Prevention of Blacktongue of Dogs. W. H. Sebrell, R. H. Onstott, H. F. Fraser and F. S. Daft, Washington, D. C.—p. 355.
Content of Reduced Ascorbic Acid in Blood Plasma in Infants, Especially at Birth and in the First Days of Life. P. W. Braestrup, Iowa City.—p. 363.
Change in Total Energy Metabolism of Rats Receiving a Diet Deficient in Inorganic Constituents. M. Kriss and A. H. Smith, New Haven, Conn.—p. 375.
Oxidative Changes Induced by Mineral Deficient Diet. M. Kriss and A. H. Smith, New Haven, Conn.—p. 385.
Anomalies in Bio-Assay of Vitamin D Milk. K. Morgareidge and B. O'Brien, Rochester, N. Y.—p. 395.

New Jersey Medical Society Journal, Trenton

35: 585-648 (Oct.) 1938

*Treatment of Myoma Uteri. T. B. Lee, Camden.—p. 590.
Endogenous Infections of the Eye, Particularly Uveitis. C. H. Schlichter, Elizabeth.—p. 594.
Treatment of Endogenous Infections of the Eye. E. S. Sherman, Newark.—p. 596.
Buried Grafts Used to Repair Depressions in the Brow, Eye Socket, Skull and Nose. L. A. Peer, Newark.—p. 601.
Water Balance from the Laboratory Point of View. J. W. Gray, Newark.—p. 606.
Induction of Labor: Maternal Welfare Article Number Thirty. R. A. MacKenzie, Asbury Park.—p. 611.

Treatment of Myoma Uteri.—Lee states that of the last 3,000 cases admitted to the gynecologic service of the Cooper Hospital 500 have been cases of fibromyoma. Myomectomy was performed in twenty. This is the preferred method of treatment whenever possible. It has been most useful in pregnancy complicated by fibroid. Myomectomy should always be done in submucous fibroids in the nonpregnant young patients. The author considers extensive adnexitis, very large tumors and nearness to the approaching menopause contraindications to myomectomy. When indicated, the morbidity and mortality of myomectomy are negligible. Subtotal hysterectomy was performed in 385 cases. The mortality and morbidity of subtotal hysterectomy are low owing to the fact that the technic has been simplified and standardized in recent years. Total hysterectomy was done in five cases. The total operation is done when malignant manifestations in the cervix are suspected. In other cases the cervix, after receiving proper treatment, may safely remain. Amputation, tracheloplasty or the cautery may be used to accomplish this purpose, although tracheloplasty is preferred in the average case. In selected cases vaginal hysterectomy is undoubtedly a procedure of choice, with a low mortality and most gratifying convalescence. Its use should be restricted to those cases in which there has been no history of severe pelvic infections and in which neither the uterus nor the adnexa appear fixed by adhesions. Total vaginal hysterectomy is indicated for very stout persons, for old persons with a small tumor, for patients who have no history of severe pelvic inflammation, in procidentia when removal of the uterus is desirable and in suspicious conditions of the cervix with fibromyoma with a roomy pelvis. Vaginal hysterectomy for the removal of large fibroids is to be deplored. When radium is used the tumor should not be larger than a three months pregnancy, it

should not be pedunculated, there should be no pressure symptoms on the bladder or the intestine, there should be no history of recent pelvic inflammation and the patient should be at or near the menopause or older. Radium was used in fifty-four cases of the present series. The symptom for which radium has been used is uterine bleeding and no reirradiation has been necessary. The reduction in the size of the tumor averages about one third and requires about one year to be complete. X-ray irradiation has little place in the treatment of fibroids. It should be reserved for inoperable cases, cardiac or otherwise and in some tumors too large for radium. Small fibroids which do not give rise to symptoms should be left alone. Many of these grow slowly and never attain sufficient size to menace the patient's health. They practically all tend to retrogress at the menopause. A malignant growth in the fundus was encountered in four of the 500 patients. Five patients died, one each from hemorrhage, septicemia, coronary thrombosis, peritonitis (complicating cancer of the rectum) and diabetes.

Pennsylvania Medical Journal, Harrisburg

42: 1-96 (Oct.) 1938

Serum Therapy of Pneumococcic Pneumonias. J. G. M. Bullowa, New York.—p. 17.
Functions of the Special Examining Boards. P. Titus, Pittsburgh.—p. 22.
Sight-Saving Classes. M. E. Smukler, Philadelphia.—p. 24.
Simmonds' Disease: Case Report. C. Rea and P. A. Hoover, York.—p. 27.
Psychology in Medicine. J. A. Cammarata, Danville.—p. 31.
*Dyspnea in Anthracosilicosis: Clinicopathologic Study. R. Charr and J. W. Savacool, White Haven.—p. 35.
The Organization and Function of a Physical Therapy Department in a General Hospital. B. S. Troedsson, Bryn Mawr.—p. 39.
Backache in Women. J. B. Raddin, Hazleton.—p. 43.
Diagnosis and Treatment of Anorectal Fistulas. H. E. Bacon, Philadelphia.—p. 45.
Injection Treatment for Varicose Veins in Lower Abdomen. E. F. McLaughlin, Philadelphia.—p. 51.
Return of Electrocardiogram to Normal in Coronary Thrombosis with Nine-Lead Serial Electrocardiographic Studies. V. A. Digilio, J. A. Pescatore and J. B. Wolffe, Philadelphia.—p. 53.
Undulant Fever: Report of Treatment of Three Cases with Mixed Typhoid Vaccine Intravenously. L. E. Etter, Warrendale.—p. 58.
Hemolytic Jaundice: Report of Case. W. C. Hendricks, Brookville.—p. 61.
Insulin Hypoglycemia in Schizophrenia. R. W. Staley, Pittsburgh.—p. 63.

Dyspnea in Anthracosilicosis.—Charr and Savacool determined the vital capacity, venous pressure and pulmonary circulation in twenty cases of pure anthracosilicosis and for comparison twenty cases of tuberculosis in which there was marked collapse of one lung under artificial pneumothorax or thoracoplasty. They found that dyspnea in anthracosilicosis is not always directly proportional to the reduction of the vital capacity while it is to the length of the pulmonary circulation time. In fact it appears that this dyspnea is largely due to cardiac insufficiency. Myocardial degeneration is a common observation in anthracosilicosis and is due to pulmonary fibrosis, emphysema and pulmonary arteriosclerosis, which are almost always present. When an anthracosilicotic patient is studied for compensation, possible myocardial insufficiency as well as the pulmonary damage should be determined. For such study the estimation of the velocity of the pulmonary circulation may give aid.

Public Health Reports, Washington, D. C.

53: 1733-1774 (Sept. 30) 1938

Mottled Enamel Survey of Bauxite, Ark., Ten Years After a Change in the Common Water Supply. H. T. Dean, F. S. McKay and E. Elvove.—p. 1736.

53: 1775-1816 (Oct. 7) 1938

*Report of Two Cases of Rocky Mountain Spotted Fever in Ohio. M. L. Cooper, M. A. Kurzner, Armine T. Wilson and R. E. Dyer.—p. 1775.
Simple Method of Concentrating Vitamin E. C. G. Mackenzie, Julia B. Mackenzie and E. V. McCollum.—p. 1779.

Rocky Mountain Spotted Fever in Ohio.—Cooper and his associates report the histories of two patients who were bitten by ticks and who later had extensive generalized macular-papular-petechial rashes which also involved the palms in both patients and the soles in one. Both patients showed definite Weil-Felix agglutination reactions. One patient died. A strain isolated from the patient who died was proved to be Rocky Mountain spotted fever by studies in laboratory animals.

Rocky Mountain Medical Journal, Denver

35: 745-832 (Oct.) 1938

Useful Hints in Diagnosis and Treatment of Gastrointestinal Disease. W. C. Alvarez, Rochester, Minn.—p. 770.
Alar Scapula. P. M. Schunk, Sheridan, Wyo.—p. 776.
Sterile Obstetric Package. Ruth E. Phillips, Denver.—p. 778.
*The Need for Prolonged Sulfanilamide Therapy in Certain Infections. G. R. Alpert, New York, and R. P. Forbes, Denver.—p. 779.
Sulfanilamide Therapy in Otolaryngology. H. L. Hickey, Denver.—p. 782.

Prolonged Use of Sulfanilamide.—Alpert and Forbes contend that severe streptococcic and meningococcic infections, such as otitis, cervical adenitis, sinusitis, mastoiditis and involvement of the meninges, demand intensive and prolonged administration of sulfanilamide if relapses are to be obviated. In a series of 200 children given sulfanilamide therapy by one of the authors relapses occurred in approximately 7 per cent. Otitis and cervical adenitis were the most frequent complications tending to relapse and required prolonged administration of sulfanilamide. Impetigo contagiosa yields promptly to sulfanilamide, but relapses are not infrequent following courses of from three to five days of the drug. Severe toxic effects of sulfanilamide can be avoided if the leukocyte count, the hemoglobin percentage and the concentration of sulfanilamide in the blood are determined daily for patients receiving large doses of the drug. The rationale for continuous treatment can be found in the mode of action of the drug. It is now generally agreed that the action of sulfanilamide is mainly that of bacteriostasis and not that of a bactericide.

South Carolina Medical Assn. Journal, Greenville

34: 251-278 (Oct.) 1938

Acute Perforation of Gastric and Duodenal Ulcers. G. H. Bunch, Columbia.—p. 251.
Congenital Narrowing of the Ileum: Report of Case. G. D. Johnson, Charleston.—p. 256.

Southern Medical Journal, Birmingham, Ala.

31: 1043-1116 (Oct.) 1938

Diverticulum of the Female Urethra. H. H. Young, Baltimore.—p. 1043.
Plastic Surgery of the Nose: Report of an Original Operation for Advancement of Nasolabial Fold. B. Douglas, Nashville, Tenn.—p. 1047.
Treatment of Malignancy with Small Radium Needles Combined with X-Ray. R. H. Crockett, San Antonio, Texas.—p. 1053.
Aminopyrine Treatment of Rheumatic Endocarditis Associated with Active Rheumatic Infection: Preliminary Report. B. R. Heninger and G. McHardy, New Orleans.—p. 1056.
The Place of Diuretics in Congestive Heart Failure. R. Lyons, New Orleans.—p. 1059.
Chronic Brucellosis of Twenty-Five Months' Duration: Report of Case with Necropsy Findings. E. E. Menefee and Mary A. Poston, Durham, N. C.—p. 1061.
*Encephalomyelitis Complicating the Virus Infections: Report of Seven Cases. F. H. Lancaster, Houston, Texas.—p. 1063.
The Artificial Pneumothorax. M. W. Miller, New Orleans.—p. 1072.
Clinical Aspects of Gastric Hemorrhage. S. M. Copland, New Orleans.—p. 1075.
Medical Aspects of Carcinoma of the Colon, with Special Reference to the Early Diagnosis. J. Friedenwald and M. Feldman, Baltimore.—p. 1078.
The Terminal Ileum: Its Surgical Importance with Special Consideration of Selected Lesions. A. H. Storck, New Orleans.—p. 1087.
Prolapse Through the Anal Sphincters. R. L. Murdoch, Oklahoma City.—p. 1091.
Unusual Complication of Radical Antrum Operation. T. E. Fuller, Texarkana, Texas.—p. 1094.
Athetosis: Surgical Treatment: Preliminary Report of Four Cases, Three Unilateral and One Bilateral. R. M. Klemme, St. Louis.—p. 1095.
Technic for Wiring Aortic Aneurysms. R. M. Penick Jr., New Orleans.—p. 1096.
Subacromial Bursitis. J. D. Collins, Norfolk, Va.—p. 1098.
Dust: Its Effect on Man from a Medical Standpoint, with Special Reference to the Dust Bowl. J. A. Blue, Guymon, Okla.—p. 1101.
Use of Social Security Funds in Expansion of the Louisiana Public Health Program. R. W. Todd, New Orleans.—p. 1106.

Encephalomyelitis Complicating Virus Infections.—Lancaster reports seven cases of encephalomyelitis in which the etiologic factor is considered to be a filtrable virus. Three followed chickenpox, two measles, one vaccination and one mumps. Encephalomyelitis complicating any of the virus infections may show a wide variation in symptoms, but in chickenpox the particular points that stand out are (1) the infrequency of headache as a symptom, (2) a marked tendency to cerebellar disturbance and (3) favorable prognosis, both as to life and as to the absence of sequelae. Since there is a definite associa-

tion between vaccination and the consequent encephalomyelitis there can be little doubt that vaccination is etiologic, although such complications are rare. In most cases the period elapsing between the time of vaccination and the onset of nervous symptoms is fairly constant (ten days). Sequelae have been rare: the principal distinguishing point between this condition and epidemic encephalitis. In measles the prominent features are (1) the greater tendency to polymorphism of symptoms and (2) the extremely high percentage of cases showing definite and permanent damage to the nervous system. In measles as well as in the other conditions the severity of the primary illness is not a determining factor in the occurrence of complications or the severity of the complications when they appear. In mumps probably the most common complication is that of meningeal irritation, and the symptoms follow closely those of true meningitis. In the case reported the noteworthy feature was the myelitis, which comes under the rarer forms of neurologic complications in this disease. The prognosis is favorable with an exceptionally low mortality and a tendency to a complete recovery and in those cases showing only meningeal symptoms the course of the illness is brief.

Southwestern Medicine, El Paso, Texas

22: 391-428 (Oct.) 1938

Surgical Shock. D. L. Secrist, Tucson, Ariz.—p. 391.
Management of Bowel Obstruction. D. F. Monaco, Gallup, N. M.—p. 393.
Subinvolution of the Uterus. G. Heusinkveld, Denver.—p. 397.
Ectopic Pregnancy. L. M. Miles, Albuquerque, N. M.—p. 401.
Fractures of Forearm and Lower Leg. L. W. Breck, El Paso, Texas, and C. Basom, Rochester, Minn.—p. 404.
Lead Absorption and Lead Poisoning: II. J. Rogde, El Paso, Texas.—p. 407.

Surgery, Gynecology and Obstetrics, Chicago

67: 413-576 (Oct.) 1938

*Alternation of Blood Supply as Cause for Normal Calcification of Bone. H. C. Blair, Portland, Ore.—p. 413.
Salivary Gland Tumors. N. W. Swinton and S. Warren, Boston.—p. 424.
Acute Safety of Ether, Divinyl Ether and Chloroform in Production of "Obstetric Degree" of Analgesia. W. B. Draper and R. W. Whitehead, Denver.—p. 436.
Swollen Atrophic Hand. A. Oppenheimer, Beirut, Syria.—p. 446.
Normal and Pathologic Developments from Cells Lining Graafian Follicle. W. S. Gardner, Baltimore.—p. 455.
Scoliosis. S. Kleinberg, New York.—p. 467.
Renal Function Tests in Differentiation of Bright's Disease from So-Called Specific Toxemia of Pregnancy. L. C. Chesley, Jersey City, N. J.—p. 481.
Blood Volume and Hemoglobin After Transfusion. W. L. Sibley and J. S. Lundy, Rochester, Minn.—p. 490.
Technic of Gastroduodenectomy. C. A. Pannett, London, England.—p. 495.
*Radical Treatment of Intractable Pruritus Ani. S. D. Manheim and L. J. Druckerman, New York.—p. 500.
Carcinoma of Major Vestibular (Bartholin) Gland. S. M. Rabson and L. H. Meeker, New York.—p. 505.
Technic for Transfusion of Blood into Abdominal Aorta. E. B. Tuohy, Rochester, Minn.—p. 510.
Carcinoma of Rectum and Rectosigmoid: Ligation of Internal Iliac Arteries. H. B. Keyes, New York.—p. 512.
Modified Well Leg Traction Splint and Distractor Combined. C. H. Watt, Thomasville, Ga.—p. 515.
Aberrant Pancreatic Tissue in Gastrointestinal Tract: Report of Two Cases and Review of Literature. M. Danzis, Newark, N. J.—p. 520.
Reliable Control for Steam Sterilization. C. W. Walter, Boston.—p. 526.

Blood Supply and Calcification of Bone.—Blair states that disuse is known to produce rarefaction and bone atrophy. This rarefaction is due to the absorption of the mineral elements of bone. The cellular constituents remain and as activity is resumed the complicated bone salt is replaced. Activity is due to one thing only—the contraction and relaxation of muscles controlling the extremity involved. Ischemia, even slight, will produce a localized acidosis in the pressure area. The change toward the acid reaction and toward the alkaline side appears to be accomplished quickly and by very little change in the blood supply. By the contraction and relaxation of muscles it would seem that these changes could be brought about in bone. It does not seem possible that reossification of bone is produced in any other way; weight bearing and stress and strain can be ruled out because even the slight activity of a person confined in bed will prevent the atrophy of the bone or bones of a limb not encased in plaster. Alternating ischemia and hyperemia can produce a comparative alternation in the hydrogen ion content of tissue fluids. It is assumed that during a rest period when muscles are relaxed, particularly just after exercise, when arterial flow is markedly increased, a swing toward the alkali side is taking place. Phosphatase acts best in hydrolysis of the phosphoric ester in an alkaline medium. At this period inorganic phosphates should increase in the tissue fluids. Muscular contraction taking place produces an ischemia, a lower hydrogen ion concentration, and as a more acid reaction develops more calcium is ionized and the tissue fluids are able to hold in solution a higher supersaturation of calcium. As muscular relaxation takes place and the swing is again toward a higher hydrogen ion concentration, the law governing salts that are soluble with difficulty causes a precipitation of the complex bone salt, composed of calcium carbonate and calcium phosphate. Theoretically it would seem that the clinical use of alternating suction and pressure, by increasing and diminishing the blood supply to the part by contraction and relaxation of the muscles, might aid in the production of union.

Treatment of Intractable Pruritus Ani.—Manheim and Druckerman excised completely all the diseased tissues in three cases of severe and intractable pruritus ani accompanied by advanced cutaneous changes. The operation is as follows: The sphincter is gently dilated, not divulsed. The entire affected area is circumscribed by a circular incision, which usually is at a radial distance of from 2 to 3 inches from the anal margin. The incision is carried down through the entire thickness of the skin until normal subcutaneous fat is encountered. The dissection is then continued in the subcutaneous tissue up to the mucocutaneous junction. The fibers of the corrugator cutis ani muscles are severed, and the subcutaneous portion of the external sphincter muscle is carefully exposed and protected. The cone shaped area of the skin is then split anteriorly and posteriorly in order to facilitate the subsequent section at the mucocutaneous junction, which is performed after clamps are placed on the mucous membrane to prevent retraction. The gluteal skin is mobilized for a distance of from 1 to 2 inches. All bleeding points are carefully controlled. Four silk mattress sutures are placed between the mucous membrane and the cutaneous edges at equidistant points anteriorly, posteriorly and laterally. Interrupted silk sutures are used to complete the approximation. A small piece of petrolatum gauze is inserted into the newly constructed anal canal and the entire operative area is covered with it. The results were gratifying. Pruritus disappeared immediately after operation. Surprisingly little pain was present throughout the convalescence. Complete healing occurred in from six to ten weeks. All three patients have been completely relieved and have remained so for from four to twenty-two months after operation. The method is not recommended for the treatment of the usual case of pruritus ani but only for long standing, intractable pruritus ani, particularly when accompanied by pronounced and possibly premalignant cutaneous changes.

Virginia Medical Monthly, Richmond

65: 583-650 (Oct.) 1938

Incidence and Importance of Human Intestinal Parasites in Tidewater, Virginia. W. B. Martin, Norfolk.—p. 585.
Undesirable Effects Following Use of Sulfanilamide. C. C. Haskell, Richmond.—p. 587.
Diagnosis and Treatment of Acute Head Injuries. J. M. Meredith, University.—p. 591.
Epididymitis. J. A. Grendeske and W. M. Brunet, Chicago.—p. 598.
Etiology of Malignant Tumors. C. Williams, Richmond.—p. 602.
Psychologic Conditioning. P. G. Hamlin, Cambridge, Md.—p. 605.
Present Preventive Programs for Feebleminded and Mentally Ill People in Virginia. J. N. Williams, Richmond.—p. 609.
Problems of the Rural Physician of Yesteryear. L. Holladay, Orange.—p. 611.
Carbuncle of the Kidney. R. L. Ozlin, New York.—p. 614.
Anorectal Stricture of Lymphopathia Venerea. J. Parrish, Portsmouth.—p. 617.
Pyelitis: Etiology and Pathology. W. F. Burdick, Washington, D. C.—p. 621.
Id.: Symptoms, Diagnosis, Treatment. J. M. Moser, Washington, D. C.—p. 622.
Sulfanilamide: Its Uses and Dangers. F. M. Howell, Hopewell.—p. 625.
Serum Treatment of Pneumonia. C. P. Jones Jr., Newport News.—p. 628.
Treatment of Abortion. R. von Lehn Buxton, Newport News.—p. 632.
Socialized Medicine. J. E. Rawls, Suffolk.—p. 635.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

2: 691-728 (Oct. 1) 1938

Acute Appendicitis. G. G. Turner.—p. 691.
Carbohydrate Metabolism in Anesthesia: Review. R. R. Macintosh and C. L. G. Pratt.—p. 695.
*Use of Bacteriophage in an Outbreak of Institutional Dysentery. D. Haler.—p. 698.
Observations on Potency and Stability of Dick Test Toxins. H. M. Leete, J. McGarrity, F. L. Ker and J. Reid.—p. 700.
Note on Diphtheria Immunization in London. M. Sorsby.—p. 701.
Vasomotor Rhinorrhea, with Asthma, Associated with Menstruation. A. S. Hoseason.—p. 703.

Bacteriophage in Dysentery.—Haler discusses an outbreak of dysentery in an institution for blind children (population thirty-two) from a few months to 7 years of age. The first patient became ill Feb. 20, 1937. The only important symptom was a little blood in the stools. This child was not suspected of having dysentery and after being segregated for a few days was allowed to join the other children freely. The epidemic followed six weeks later, but April 22 the same child was ill again. On the latter occasion the first stool to be examined showed no dysentery bacilli, but April 25 Bacillus dysenteriae Sonne was obtained. Following this presumed first case of February 20 there were three cases on April 4 and 5, four more cases April 10 and 11, another febrile case of dysentery occurred April 18, and April 22 the first patient was again reported ill. It is possible that this patient may have harbored Bacillus sonnei from February 20 and thus have been the source of the other infections. April 25, three more cases occurred. Bacteriophage treatment was recommended for those who had been sick, those unaffected and all the staff. All those in bed and on bed isolation received dysentery bacteriophage three times daily until the stools were reported "free from Bacillus dysenteriae Sonne and from atypical dysentery bacilli." On the second day after treatment was begun, one further case occurred. This was the last; and now, more than a year later, there has been no fresh case. This sudden cessation of the epidemic may have been a coincidence, but there was nothing to suggest that the cases between April 4 and 27 were being infected from outside the home. The repeated isolation of Bacillus dysenteriae Sonne from the stools suggested that this infection was being spread. No medicinal treatment other than bacteriophage was administered.

Journal of Hygiene, London

38: 521-646 (Sept.) 1938

Leptospiral Infections in Rats: Presence of Specific Leptospiral Immune Bodies in Serum and Their Relationship to Carrier Conditions. J. Smith.—p. 521.
Bacterial Content of Ice Cream in Relation to Manufacture, Storage and Standards of Purity. Doris A. Bardsley.—p. 527.
Further Observations on Influence of Growing Family on Diet in Rural Districts in Sussex. F. Brockington.—p. 547.
Some Observations on Rideal-Walker Test. A. C. Thaysen.—p. 558.
Investigation of Normal Agglutinins for Typhoid and Paratyphoid Bacilli in Human Serums in Victoria and Interpretation of Widal Test. T. S. Gregory and Nancy Atkinson.—p. 566.
Mortality of Hemolytic Streptococcus on Skin and on Other Surfaces. J. M. L. Burtenshaw.—p. 575.
*Growth of Salmonella Typhi and Certain Other Members of Salmonella Group in Milk and Butter Stored at Atmospheric Temperatures. E. J. Pullinger and Audrey E. Kemp.—p. 587.
Study of English Diets by Individual Method: III. Pregnant Women at Different Economic Levels. R. A. McCance, E. M. Widdowson and C. M. Verdon-Roe.—p. 596.
Experiments on Staphylococcic Food Poisoning. F. C. Minett.—p. 623.
Adsorbent Effects of Various Dusts on Diluted "Old Tuberculin." S. L. Cummins and Enid M. Williams.—p. 638.

Salmonella in Milk and Butter.—The experimental results of Pullinger and Kemp show that the Salmonella which is likely to contaminate milk supplies and which causes either typhoid or food poisoning in man grows readily in freshly drawn milk stored under normal commercial or household conditions when refrigeration is not resorted to. Any effect exerted by the growth-inhibitory factor of fresh milk is transient, since multiplication was observed even after small initial inoculums had been added to the milk. The inhibitory factor was not bactericidal for Salmonella. Whether contamination originates from the cow, as usually happens with Salmonella dublin, or from some external source as with Salmonella typhi, the really important factor in the epidemiology of milk borne Salmonella outbreaks is that the contaminating organism can thrive during storage and thus cause wholesale contamination of pooled milk. A point of some interest which has arisen out of the investigation is the fact that strains of Salmonella typhi recently isolated from human cases multiplied more rapidly in milk than did old laboratory stock cultures. When artificially incorporated in butter after manufacture, these organisms were found to survive for periods varying from two to three months and even longer when the butter was stored at 15 or 3 C. Neither the quality of the butter nor the presence or absence of salt appeared to influence this survival. There was no suggestion that any multiplication occurred, and after about two months' storage the organisms began to decrease in numbers.

Journal of Physiology, London

93: 305-438 (Sept. 16) 1938

Relation of Contracture to Increment in Resting Heat Production of Muscle Under Influence of Potassium. C. G. Smith and D. Y. Solandt.—p. 305.
Synchronized Impulse Discharges from Receptors in Deep Tissues in Response to Vibrating Stimulus. F. Echlin and A. Fessard.—p. 312.
Absorption of Ultraviolet Radiation by Human Sweat. W. H. Crew and C. H. Whittle.—p. 335.
Phase Angle of Normal Human Skin. A. Barnett.—p. 349.
Study of Source of Liver Fat Using Deuterium as an Indicator. H. M. Barrett, C. H. Best and Jessie H. Ridout.—p. 367.
Accuracy of Thermostromuhr Method for Measuring Blood Flow. H. Barcroft and W. M. Loughridge.—p. 382.
Experiments on Relation Between Thyroid Gland and Lactation in the Rat. S. J. Folley.—p. 401.
Maximal Growth Rate of Capon Comb. C. W. Emmens.—p. 413.
Some Effects of Compounds of Androsterone-Testosterone Series on Ovariectomized Mice. C. W. Emmens.—p. 416.
Effect of Subarachnoid Administration of Histamine on Rate of Absorption of Isotonic Saline Solution in the Dog. T. H. B. Bedford.—p. 423.
Effect of Hypertonic Solutions on Gastric Secretion and Intra-Ocular Pressure. R. L. Noble and J. D. Robertson.—p. 430.

Lancet, London

2: 761-812 (Oct. 1) 1938

The Heart Sounds in Normal and Pathologic Conditions. E. Braun-Menendez.—p. 761.
Duration of Action of Zinc Protamine Insulin. R. S. Aitken.—p. 768.
*Air Embolism: Reports of Three Cases. G. R. Osborn and J. C. C. Dawson.—p. 770.
Carcinoma of the Tongue: Late Results of Treatment. R. Phillips.—p. 772.
Osteomalacia of Spine Following Abuse of Laxatives. E. Meulengracht.—p. 774.

Air Embolism.—Osborn and Dawson report three cases of air embolism: two complicating labor at full term free from infection (in each the postmortem examination was made before decomposition could complicate the observations) and one of a boy aged 16. None had been treated with chemicals. At necropsy both women showed definite fatty changes in the liver, a condition often found in unexpected deaths. In the first case the severity of this change may have been the reason for the extraordinary atonicity of the uterine muscle. The histories of the two women from the time the air presumably gained access to the veins is strikingly similar and the times taken to die (three and one and one-half hours) are noteworthy. The liver and alimentary tract in the third case appeared normal. The kidneys showed a severe chronic nephritis which was evidently responsible for the cardiac hypertrophy. The renal pelves and ureters were normal. The bladder was empty; there was a hemorrhage of about 60 cc. into the tissues to the left of it, which was not connected with the much larger hemorrhage into the mediastinal tissues. There was no tear of the bladder or injury of the rectum. According to the mother, the boy seemed all right when he got out of bed to pass urine, so that much of the blood present in the pleural cavity was probably the result of postmortem bleeding. Air embolism presents characteristic symptoms. These are sudden onset, disappearance of the pulse, deep respirations with air hunger, restlessness with chest discomfort (shown especially by lashing about with the arms) pallor if the case is immediately fatal, associated with fright and cyanosis if death is delayed. If the condition should be recognized during life it is conceivable that aspiration of the right side of the heart would avert a fatal issue.

Journal de Médecine de Lyon

19: 527-554 (Sept. 20) 1938

*Etiology of Angina Pectoris. L. Gallavardin.—p. 527.

Etiology of Angina Pectoris.—The anginal syndromes which are the object of this study by Gallavardin are those of true angina of coronary origin. This statistical report, which is based on approximately 1,900 cases, reveals that angina pectoris is much more frequent in men than in women, the ratio being about 4:1. The onset of the anginal symptoms is most frequent in persons between the ages of 45 and 65 years; that is, in nearly 75 per cent of the cases the onset occurs during those years. The role of syphilis is important but limited and the author thinks that formerly the significance of syphilis in angina pectoris was greatly exaggerated. The proportion of syphilitic patients (certain and doubtful cases) does not exceed 20 per cent of the total number of patients with angina pectoris. However, the influence of this infection is the more evident, the younger the patients are: it plays a part in not far from 50 per cent of those under 35, in nearly 40 per cent of those under 40 and in nearly 25 per cent of those under 50. In those above the age of 50 the incidence decreases rapidly to from 15 to 18 per cent for men and to from 5 to 8 per cent for women. The author says that nicotine is not the only cause of nonsyphilitic angina pectoris. Of the men with nonsyphilitic angina pectoris, more than 20 per cent had never smoked; if the women are included, the percentage of nonsmokers exceeds 40. Coronary angina pectoris by itself has nothing in common with arterial hypertension. In the author's material more than 60 per cent of the men had a tension which did not exceed 160 mm. of mercury. However, the coexistence of the two disorders is quite common in women as well as in men. It is even possible that certain hypertensive states provoke, especially in women, the appearance of an anginal syndrome which does not depend on coronary lesions.

Presse Médicale, Paris

46: 1449-1464 (Oct. 1) 1938

*Buccal Cacosmias. G. Sanarelli.—p. 1449.
Hemorrhagic Rectitis. P. Oury and R. Stieffel.—p. 1452.

Buccal Cacosmias.—Sanarelli says that halitosis, or buccal cacosmia, has nothing in common with the enteropulmonary gaseous exchange, by which the odors of certain ingested substances may be temporarily noticeable in the expired air. Buccal cacosmia is not a transitory condition but a permanent disorder, which frequently exerts a harmful influence on the psyche of the patient. Medical science has ascribed it to banal causes such as digestive irregularities or poor condition of the teeth. The buccal cacosmia with which the author is concerned in this report is of the "essential" type, which should not be confused with the halitosis of persons who have acute or chronic inflammatory processes with a pulmonary or buccopharyngeal localization such as pulmonary abscess, bronchiectasis, sinusitis, mercurial stomatitis, chronic tonsillitis or dental pyorrhea. He applies the term essential buccal cacosmia to the permanent halitosis in persons who otherwise appear healthy. Reviewing the hypotheses on the origin and nature of essential buccal cacosmia, he mentions those of Boldyreff and of Tamches. He directs attention to the antimicrobic action of saliva, which he demonstrated as early as 1892 and which was confirmed by other investigators. Further he describes his more recent studies on the bacterial flora, directing especial attention to the antiputrefactive action of the buccal streptococci. After describing several of his experiments on the bacterial origin of essential buccal cacosmia, he says that the results are always the same; that is, the buccal streptococci in the presence of even small quantities of carbohydrates succeed always by means of their acidifying diastases to impede the development (in the buccal cavity as well as in vitro) of other species of micro-organisms, including the putrefactive ones. If carbohydrates are lacking, the bacteria of putrefaction become predominant and in the presence of proteinic substances give rise to fetid odors. In the further discussion the author points out that, owing to the mild antimicrobic action of the saliva, the continuous salivary irrigation of the buccal mucosa tends to reduce the abundant development of the oral bacterial flora. However, if the buccal or intestinal secretions undergo changes, the conditions become favorable for a free and abundant development of the bacterial flora. The author thinks that this is the reason why patients with disturbances of the digestive tract, who lack appetite and are nauseated, often have a fetid breath. These are the pathologic conditions of the stomach which exercise an indirect influence on the buccal mucosa and consequently on the salivary secretions. In the conclusion the author emphasizes once more that the origin of buccal cacosmia is not gastric, intestinal, pulmonary or due to particular microbes giving off the fetid odors. It is entirely local, being caused by banal putrefactive fermentations, which manifest themselves in the buccal cavity under the aforementioned abnormal local or general conditions.

Revue Belge des Sciences Médicales, Louvain

10: 341-392 (June-July) 1938

*Clinical and Biologic Study of Pleural Effusion in Patients with Cirrhosis. M. Goffart.—p. 341.
Physicochemical Modifications of Blood After Surgical Interventions Under Various Anesthetics. I. Blitstein.—p. 371.

Pleural Effusion in Patients with Cirrhosis.—Goffart reviews the clinical histories of ten cases of pleural effusion in cirrhosis and then gives his attention to the pathogenesis. In conclusion he states that the pleural effusions are frequent in patients with cirrhosis. The appearance and evolution of pleural effusion is hardly noticeable and it must be searched for carefully in the course of the examination. The physical signs are deceiving, the roentgenologic examination underestimates the quantity of liquid and an exploratory puncture is necessary to settle the doubt. The pleural effusion does not aggravate the prognosis, except for septic complications. The effused fluid is relatively poor in albumin, fibrin and cholesterol. Its cytology is mixed; it always contains blood and the chloride content is increased. The pathogenesis is complex and it is unquestionably justifiable to invoke the mechanical causes of pulmonary stasis by elevation of the diaphragm; the reduction of the osmotic power of the proteins by inversion of the albumin/globulin ratio of the serum, and the impaired functional activity of the capillaries. The author says further that tuberculosis must still be regarded as a possible causal factor of pleurisy, but he did not detect it as a cause in the cases which he observed.

Schweizerische medizinische Wochenschrift, Basel

68: 1133-1152 (Oct. 8) 1938

Hemorrhagic Pleurisy in Children. Taillens.—p. 1133.
Pathogenesis and Therapy of Rheumatism. C. Haffter.—p. 1134.
Gold Therapy in Chronic Articular Rheumatism. W. Tschopp.—p. 1136.
Diagnosis of Adnextuberculosis. E. Held.—p. 1139.
*Experimental Transmission of Poliomyelitis to Cattle. E. Frauchiger and W. Hofmann.—p. 1140.

Experimental Transmission of Poliomyelitis to Cattle.—Frauchiger and Hofmann cite Frauchiger's report about a case of spontaneous poliomyelitis in a heifer (THE JOURNAL, July 2, 1938, p. 74). This observation induced them to attempt the transmission of poliomyelitis to cattle, although it was generally believed that monkeys were the only animals that could be inoculated with this disease. Poliomyelitis material from human subjects (brain and spinal cord) was inoculated into three heifers aged between 12 and 18 months. Since it was the first aim to determine whether the inoculation would take, large doses were given and the material was introduced by three different routes (intranasal, intraperitoneal and intraspinal). Only one of the animals was not subjected to the intraspinal administration. Besides increases in temperature at the onset, there were no general symptoms such as gastrointestinal disturbances, nasal discharge and sweating. Moreover, there were no signs of meningeal irritation (stiffness of the back). However, after two or three days signs of paralysis appeared on the extremities, particularly the posterior ones. The paralytic symptoms increased to the seventh day. In one of the animals they persisted in about the same intensity, whereas in another one they disappeared, but never completely.

During the severest stage of the disease the animals had an atactic walk and frequently fell down. Completely flaccid paralysis was not observed. The third animal, which had not been subjected to intraspinal inoculation, showed a mild paresis which soon disappeared again. The walk and the behavior of the animals were recorded on a kinematographic film. In the fourth week after the inoculation, bilateral atrophy of the gluteal musculature was observed in one of the animals. In another animal atrophies were observed in the musculature of the pelvis and thighs as well as on the right foreleg. Examination of the cerebrospinal fluid of the animals revealed changes indicative of organic disease of the central nervous system, but since microscopic studies have not been made as yet the authors are unable to state whether the disease process is identical with that of poliomyelitis. However, further investigations will be devoted to such microscopic studies and to attempts to transmit the disease further by means of material obtained from these animals.

Annali di Ostetricia e Ginecologia, Milan

60: 863-1007 (Aug. 31) 1938. Partial Index

Diagnosis of Malformation of Uterus by Metrography. E. Bortini.—p. 863.
Clinical Study of Treatment of Some Gynecologic Diseases by Androgen (Testosterone Propionate). A. Migliavacca.—p. 943.
*Treatment of Puerperal and Postoperative Thrombosis and Thrombophlebitis of Legs. C. Pardella.—p. 973.
Kustallow's Reaction on Infusoria in Biologic Diagnosis of Normal and Ectopic Pregnancy. V. Pugliatti.—p. 991.

Treatment of Thrombosis and Thrombophlebitis.—Pardella reports satisfactory results of hirudinization (local application of leeches) and application of a bandage of wide adhesive tape in twelve cases of puerperal and postoperative thrombosis and thrombophlebitis of the legs. The leg is raised to about 40 degrees for a few minutes, during which the joints of the ankle and knee are covered with a thin layer of cotton and the bandage is applied from the distal end of the middle third of the foot up to a point near the root of the thigh. Compression and tension of the bandage are moderate and uniform. The toes are not included in the bandage, which is applied in such a manner that the lower half of each new turn of the adhesive tape covers the upper half of the turn previously applied. Immediately after application of the bandage, the patient is asked to perform a few slight movements of flexion and extension and the limb is placed at rest. Four or six leeches are placed at the anterolateral aspect of the thigh near its root. They are changed two or three times at intervals of twenty-four hours in septic thrombophlebitis and discontinued after the first application of twenty-four hours in simple thrombosis. A few moments are spent in flexion and extension on the sixth and ninth days of application of the bandage. According to the author the immobilization of the local venous system induced by the bandage results in normalization of the local venous and lymphatic circulations with consequent reabsorption of edema, improvement of the nutritional conditions of the tissues and rapid control of the disease. The patients are relieved from the first day. The treatment lasts for from nine to thirteen days, according to the evolution of edema, pain and the general symptoms. The satisfactory results are permanent, as verified by the author through further observation of the patients.

Giornale Veneto di Scienze Mediche, Venice

12: 421-484 (Aug.) 1938. Partial Index

*Residual Pain After Appendectomy: Surgical Intervention. G. Pieri.—p. 421.
Subcutaneous Traumatic Rupture of Common Tendon of Brachial Biceps Muscle. M. Tommasini.—p. 431.
Tetanus in Newborn Infant: Favorable Results of Serum Treatment. G. Giomo.—p. 440.
Thoracentesis and Pneumothoracentesis in Common Practice. B. Boggian.—p. 446.

Pain After Appendectomy.—Pieri states that in the course of the last five years thirty-six patients have complained to him of persistent pain in the right iliac fossa after an appendectomy for either chronic or acute appendicitis. In the majority of the cases the pain began several hours after meals. The roentgen study of the cecal region failed to show any pathologic changes of the cecum. A right vertical laparotomy showed that in four cases pain was caused by the presence of postoperative adhesions, removal of which induced recovery of the patients. In thirty-two cases one of various pathologic conditions (chronic colitis, simple, tuberculous or acute typhlitis or ileotyphlitis, mobile or atonic cecum and cecal neuralgia) existed. Resection of a segment of 2 or 3 cc. of the ileocolic plexus between two ligatures and through a right vertical laparotomy induced recovery of the patients, which was verified by a follow-up observation. In Italy the operation is known by the author's name, since he is the originator. Permanent satisfactory results have been reported from several Italian hospitals.

Radiologia Medica, Milan

25: 779-880 (Sept.) 1938. Partial Index

Roentgenologic Aspects of Round Images of Pulmonary Field. L. Gallavresi.—p. 779.
*Acquired Posterior Sinistrocardia and Special Deformation of Trachea: Further Study. G. Giordano.—p. 820.
Roentgenography of Larynx in Anteroposterior Position: Technic and Results. L. Ciurlo and A. Oliveri.—p. 834.
Roentgenologic Aspect of Early and Advanced Gas Gangrene. A. Grilli.—p. 843.

Acquired Posterior Sinistrocardia.—Giordano describes a rare form of tuberculous fibrothorax with permanent lateral posterior displacement of the mediastinum and mediastinal organs, especially the heart and large blood vessels. In the roentgenograms of the thorax which are taken in the latero-lateral position, the cardiovascular shadow shows at the paravertebral region separated from the sternal wall by lung tissue. The author reports four new cases. All the patients were adults suffering from pulmonary tuberculosis with fibrothorax, which developed spontaneously or after artificial pneumothorax or a surgical operation in pleural empyema. Stabilization of fibrothorax and subsequent transposition of the heart to the left had taken place in all cases during either youth or childhood. All had acute bronchiectasia. Bronchography showed that the lower and middle lobes of the lung were emphysematous and displaced to the left, between the sternal wall anteriorly and the cardiovascular shadow posteriorly. The esophagus, especially the thoracic segment, was dilated and retracted to the back in two cases and to the left in two cases. There was no stricture of the esophagus. The trachea, its bifurcation and the left bronchi were displaced to the left and greatly dilated and deformed in two cases, in one of them to a large extent. The author advises further study of the subject in order to determine the mechanism of production of the special displacement of the mediastinum and mediastinal organs in this form of tuberculous fibrothorax.

Klinische Wochenschrift, Berlin

17: 1353-1384 (Sept. 24) 1938. Partial Index

Comparative Investigations on Methods for Determination of Capillary Resistance. T. Jersild and A. Elmby.—p. 1359.
Question of Benign Lymphocytic Meningitis. H. Glatzel.—p. 1360.
Coli-Infection (Colibacillosis of Duodenum). W. Grunke.—p. 1362.
*Physiology and Pathology of Intermediary Fat Metabolism: Influence of Succinic Acid on Diabetic Ketosis. F. Müller and H. Buchwald.—p. 1364.
Experimental Production of Lipomatosis. K. Kuré, T. Sahara and S. Okinaka.—p. 1366.
Value of Pallida Reaction According to Gaehtgens for Serologic Examination of Cerebrospinal Fluid for Syphilis. T. M. Vogelsang.—p. 1370.

Influence of Succinic Acid on Diabetic Ketosis.—Müller and Buchwald state that the literature contains contradictory reports about the effect of succinic acid on diabetic ketosis and so they decided to investigate this problem on a considerable number of their patients. In doing this they not only determined the elimination of ketone bodies in the urine but also examined the ketone content of the blood several times each day. Summarizing their observations, they state that the clinical examination of the succinic acid therapy of diabetic ketosis, which was recommended by Koranyi and Szent-Györgyi, revealed that the oral administration of succinic acid, even if continued for weeks, does not compensate a diabetic acetonuria. They did not even observe a temporary reduction in the daily ketonemic curve.

Moreover, the typical ketonemic curve observed in diabetic patients, after they have been subjected to a fat tolerance test, could not be influenced in the antiketogenic direction by the administration of succinic acid.

Münchener medizinische Wochenschrift, Munich

85: 1465-1496 (Sept. 23) 1938. Partial Index

Permanent Results After Transurethral Electrosurgical Resection of Prostate. B. Reiser.—p. 1467.
*Relations Between Varicella and Herpes Zoster. V. Hourand.—p. 1468.
Poisoning Caused by Extract of Arnica in Alcohol. O. Merdinger.—p. 1469.
Method and Aim of Psychotherapy. M. H. Göring.—p. 1472.
Impairment of Procreative Capacity Following Injection Therapy of Hernia. R. Goldhahn.—p. 1475.

Relations Between Varicella and Herpes Zoster.—Hourand reports the clinical history of a woman aged 50. He regards this case as important in connection with the problem of the relation between varicella and herpes zoster. The woman developed herpes zoster with the typical symptoms: strictly localized vesicles of various sizes, reddishness and swelling of the skin with great painfulness; the left eye was involved. This attack of herpes zoster was followed a few days later by varicella. The author reviews the literature on the relation between varicella and herpes zoster, citing the concurrence of these two disorders in the same cases but also the development of varicella in persons who had come in contact with persons having herpes zoster and vice versa. After mentioning serologic and immunologic investigations on the etiologic relation between the two disorders, he says that several authors reject the identity of the viruses of varicella and herpes zoster. Some cite the successive appearance of varicella and herpes zoster after intervals of several months as evidence against such an identity but others believe that in such cases the causal agent of varicella, as a dermatotropic virus, confers immunity only on the skin, whereas the neurotropic virus of herpes zoster confers immunity only on the nerves. However, this partial immunization is regarded as the exception and the general immunization as the rule. Returning to the reported case, in which herpes zoster and varicella concurred, the author says that dermatologists have referred to these cases as herpes zoster generalisatus. However, he agrees with von Bokay, Netter, Haslung and others, who reject this term, because in his patient the vesicles were not arranged along the course of certain nerves.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

82: 4295-4410 (Sept. 3) 1938. Partial Index

Myxedema of Heart. E. Behr and J. Mulder.—p. 4303.
Changes in Sensitivity of Uterus Toward Posterior Pituitary and Ergot Preparations Under Influence of Sex Hormones. J. H. Reisel.—p. 4310.
*Care for Soft Parts During Delivery by Practitioner. J. Baart de la Faille.—p. 4315.

Care for Soft Parts During Delivery.—Baart de la Faille assumes an antagonism between the uterus and the soft parts during delivery. The violent pain of the period of dilatation is only partly the result of the uterine contractions. Anxiety and cold cause an extremely painful spasm and this inhibits the labor pains and the dilatation of the os, real rigidity of the os being extremely rare. By adequate heating of the bed and the room, much pain can be saved; the same applies to the use of antispasmodics and analgesics. The author found that with the increasing variety of these drugs the uterine action can be utilized to full advantage, weakness of uterine contractions occurring far less and solution of posterior pituitary being only rarely required. The first stage of labor, the period of dilatation, can be shortened in a considerable percentage. The uterine contractions during expulsion, although less painful, likewise are acted on favorably by these medications, the difficulties of expulsion becoming far less if nature is left to have its own way. The process of distending the soft part thus becomes much more gradual and the indication for extraction by forceps becomes much less frequent. Among the results of excessive distention the author differentiates prolapse from rupture, the former ensuing after forcible distention of the pelvic diaphragm, the latter being limited to the perineum. Slow distention of the pelvic diaphragm prevents a prolapse and slow dilation of the vulval ring reduces the danger of a rupture and the necessity of a suture. The author is skeptical of the value of suturing the perineum. However, he emphasizes that lifting of heavy objects should be avoided for six weeks after delivery.

Hospitalstidende, Copenhagen

81: 861-888 (Sept. 6) 1938

Acute Porphyria Originated During Hospitalization: Case. A. Eldahl.—p. 861.
Porphyrines and Clinically Applicable Methods for Their Establishment. A. Eldahl.—p. 864.
*Symptomatology of Acute Porphyria and Classification of Porphyrinurias. A. Eldahl.—p. 871.
Essential Fibropenic Hemorrhagic Diathesis. N. I. Nissen.—p. 879.

Acute Porphyria and Porphyrinurias.—Eldahl says that acute porphyria is a well defined disorder of acute onset, the main symptoms of which may be violent abdominal pain, constipation (in rare cases diarrhea), organic disorder of the cerebrum and medulla (insomnia, psychosis, multiple pareses), hepatic and renal insufficiency and elimination of porphyrin and chromogen in the urine. The symptoms of disorder of the cerebrum and medulla especially mark the disease and resemble those in encephalitis and poliomyelitis. Acute porphyria is ascribed to a congenital and hereditary anomaly in the intermediary metabolism, a latent or relative insufficiency of the porphyrin synthesis, which can often become absolute. The synthesis probably takes place in the liver. The immediate cause may be infections, often mild infections, overexertion, psychic attack or chemical substances in small amounts. The prognosis is unfavorable; the mortality is about 70 per cent. About 70 per cent of the patients are women, mostly between the ages of 20 and 30; no case under the age of 15 has been reported. Patients with porphyria are often dark skinned but without hypersensitivity to light. Anatomopathologic examinations show slight cirrhotic changes in the liver, in some cases hemosiderin deposits, acute nephritic changes in the tubuli contorti of the kidneys and interstitial leukocyte accumulations, signs of obliterating phlebitis in the kidneys and other organs, and in some cases slight hemorrhages in the cerebrum. In many cases diet treatment has been given such as was formerly generally applied in hepatic and renal disturbances; in the author's personal case of acute porphyria, which originated during hospitalization, insulin and dextrose was administered. Porphyrinurias are classified in two groups: (1) without symptoms, (*a*) familial hereditary, constant or periodic, (*b*) symptomatic, in fever, anemia and so on, (*c*) medicamental, after arsphenamine and sleeping powders; (2) with symptoms, (*a*) in porphyria, (*b*) toxic, after arsenic, lead, sleeping powders and so on, (*c*) in hydroa vacciniforme.

Ugeskrift for Læger, Copenhagen

100: 989-1014 (Sept. 1) 1938

*Are Primary Epidemic Alveolopneumonia and Psittacosis Same Disease? R. K. Rasmussen.—p. 989.
Paroxysmal Myoplegia: Case. J. E. Poulsen.—p. 998.
Plummer-Vinson's Syndrome: Case. H. Videbech.—p. 1001.

Epidemic Alveolopneumonia and Psittacosis.—Rasmussen concludes from the account of the sixty-eight cases of primary epidemic alveolopneumonia observed in the Faroe Islands in September, 1933 (Arthur A. Rasmussen, *Ugeskrift for læger,* 1934) that the disease is clinically like psittacosis and has much in common with it epidemiologically. The two diseases affect the same age group and cause about the same mortality. However, while psittacosis is a disease of fall and winter, primary epidemic alveolopneumonia occurs almost exclusively in the month of September and affects six times as many women as men, and particularly pregnant women. The incubation period is unknown. The agreement between the time of the catch of the young procellarians (storm birds) and of the incidence of primary epidemic alveolopneumonia suggests that the source of infection may be in these birds, in which case the infection must be transmitted in the plucking and cleaning of the birds. The author also calls attention to the resemblance of this disease to other disorders, such as streptococcic pneumonia and streptococcic sepsis, and in its milder form to the initial fever of tuberculosis.